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SCIENCE

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A. J. Carlson

On the Floor of the Senate

Howard A. Meyerhoff

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SCIENCE

Vol. 103, No. 2674 Friday, March 29, 1946

Is There "A Standard to Which the Wise and the Honest Can Repair"?

A. J. Carlson

Professor Emeritus of Physiology, University of Chicago

MY TITLE IS A QUOTATION from George Washington, the "father of our country," who said: "Let us raise a standard to which the wise and honest can repair; the rest is in the hands of God." The question marks are my own. My questions are: Is there such a standard? Can we agree on such a standard? Who are the wise and the honest to rally around this standard? If there be such a standard and if there be any wise and honest men, I would say the rest is in the hands of man, not in the hands of God.

Were I to follow my own dictum that a scientist should keep his mouth shut and his pen dry until he knows all the facts, I would stop with the mere quotation from George Washington. However, on the basis of my understanding of man and my acquaintance with human history, I have also advocated in the past that a man's social responsibility is commensurate with his understanding of man and nature. If that is even approximately correct, we in the natural sciences surely have no less responsibility in the present dilemma of the race than have men in business, industry, and government. The "Atlantic Charter" promised us freedom from want and freedom from fear, if the war against Germany and Japan was waged to victory for our side. We have achieved victory, but our world is now plagued with more want and more fear—and on a larger scale than ever before. This is merely another illustration that war, violence, and destruction are probably not the best means by which to establish relative freedom from want of food and fear of further violence.

Men of science, particularly our colleagues in chemistry, physics, and engineering, are *praised* and *blamed* for producing during this war better and more efficient weapons of destruction, specifically the atomic bomb. This has led, especially in the United States, to plans further to facilitate scientific research through federal-government financing, as a means for greater national security—that is, greater freedom from fear. On the other hand, there are voices, though less loud, charging that science, and the scientists, are primarily responsible for the increasing destructiveness of war and the increasing injurious effects of war on the human race, and these voices call for a moratorium on science and appeal to philosophy and religion for the answer to the dilemmas of the hour.

Before proceeding to discuss the standard George Washington had in mind and the wise and the honest who should rally around this standard, if such a standard can be found, let us dispose of some of the rather superficial accusations, charges, and fears that are current today—yes, even today, when the shooting, at least, of the worst war in human history is over.

Facing these dilemmas, not a few fellow citizens appear to substitute hysteria for history and sentiment for science. As I see it, science is as much and as definitely a part of nature as are the life-giving sunshine and the destructive tornado. To significantly or permanently retard or abolish science, we must fundamentally modify or destroy man, for science, in its final analysis, is the product of human curiosity. But temporary retardation of science can be achieved both by violence and by unwise legal or political dictation in times of peace as well as in times of war, for the processes of scientific research are not as simple as adding fertilizer and water to parched and depleted soils. In the latter case there is no problem of mental and physical freedom of the individual man, the individual scientist.

Address of the retiring president of the American Association for the Advancement of Science delivered at St. Louis, Missouri, on 27 March 1946. Ordinarily this address would have been delivered in December 1945, but due to wartime conditions this meeting was postponed to the spring of 1946.

Scientists are being urged to "knock at the door of politics." Scientists probably should do that, if in so doing we do not deviate from the path of science and continue to stick by the facts. If, when "knocking at the door of politics," we follow current political mores, we will injure science and render no service to society. Specific current examples of scientists "knocking at the door of politics" are the endeavor of American scientists to guide and improve federal legislation concerning the National Science Foundation and the organized endeavor of the American chemists, physicists, and engineers responsible for the development of the atomic bomb to foster national legislation having to do with publicity and control of atomic energy in the best interests of the future peace and prosperity of all men everywhere.

Yes, men of science are urged to "knock at the door of politics." I think that our social responsibility compels us to knock at this door, not only as individual citizens but as organized professional people. And yet Sir Josiah Stamp, former president of the British Association for the Advancement of Science, says: "The training of the scientist includes no awareness of the social consequences of his work, and the training of the statesman and administrator no preparation for the potentiality of rapid scientific advance and drastic adjustment due to it, no provision of the technical forces which are shaping the society in which he lives." Perhaps our "knocking at the door of politics" will be relatively futile until leaders in politics understand the scientific methods and the ethics of scientific research.

According to my best recollections, the standard which George Washington asked us to raise over a hundred years ago was not specifically described, but it undoubtedly related primarily to political, economic, and religious freedoms such as we usually designate under the term democracy. Certainly that standard, even raised by a leader of a rebellion, stands for peace rather than war as the human ideal toward which we must labor with all our knowledge and courage. We may also assume that George Washington's *standard* embodied the "golden rule." But as formulated by leaders of our race in the more distant past, the golden rule seems too utopian for man at the present stage of intellectual and social evolution. In international relations we usually follow the golden rule in reverse. We do unto others what we fear they are about to do to us; and if our enemy hungers, we starve him some more. But man today seems capable of such realistic application of the golden rule as is seen in open conferences, fair compromise, and honest cooperation. In international relations this formula seems at present the only substitute for war. Given even moderate understanding and integrity in our politi leaders, this procedure does not seem beyond hum capacity of any race or nation today.

But is peace, as opposed to war, a possibility the human race? It is a fact that some statesme some soldiers, some philosophers, and some fellow s entists say that intermittent wars are as inevitable a part of man's struggle for existence and as nature crude way of eliminating the less fit. If that is tru a standard looking toward a more durable pea among the human race is certainly not a standard which the "wise and the honest can repair." Th standard, the inevitableness and perennial perpetui of war, is, of course, clearly opposed to the plan an I hope, the efforts of the United Nations. If war inherent and inevitable in human nature, all effort in the plans of the United Nations are a sham, delusion, and a snare. I, for one, do not accept thi view as a scientific fact or as one rendered probabl and inevitable by scientific facts; for war has been gradually eliminated between families, tribes, and even larger groups. To be sure, we still have violent revolutions within individual nations, where it is not a matter of threat or force from without, or matters of difference in religion, race, or skin color. But in recent years, at least, and where empires cover a large part of our globe, wars are violence between nations. Eliminating this last step may be more difficult, but biologically not less possible, than eliminating war between families and tribes.

If it is true that primary drives toward war and violence are greed, vanity, and fear, it may be argued that wars are inevitable as long as greed, vanity, and fear are not controlled or somehow checked by understanding, intelligence, and a growing sense of justice. I think mankind should reckon with this fact. The control of greed, vanity, suspicion, and fear by understanding and intelligence is going to be a slow process, even through modern travel, communication, and education, as long as modern communication and education are partly sidetracked toward increasing greed, suspicion, and fear. I think we can be more positive, however, in answer to those fellow citizens (industrialists, politicians, and scientists) who argue and find comfort in the supposed fact that war is beneficial to the human race in the sense of survival of the fittest and elimination of the less fit. In modern times the less fit physically and mentally are not drafted into the armed forces in any nation, except under extreme provocations. Hence, death and mental and physical injuries in the armed forces in war falls on the physically and mentally more fit of a nation's population. As we now wage war, not against the armies and the navies of the enemy, but against men, women, and

dren of enemy countries, everyone can clearly see atomic and other bombs, gunfire, poison gas, flame wers, etc., do not discriminate between the fit and less fit; the same is true of the sequelae of war: *vation* and *epidemic disease.* In other words, dern war tends to render even the most fit less in body and mind for the functions of peace in ry nation. Even with the partial understanding the nature of man and the universe available during last hundred years, it has been possible for some the small nations to change from war to planned persistent peace, by their own understanding and ice, even without the aid of an international police ce, as is now being planned by the United Nations. own forebears, the Scandinavian vikings, were not long ago the scourge of Europe, warring, killing, robbing in every accessible land. The descendants these warriors have not waged war voluntarily for er a hundred years, but have used their energy and derstanding in the arts of peace without, so far as can judge, suffering national degeneration. Of urse, on this latter point, a hundred years is but pilot experiment. Finally, we now know enough the role of heredity and health in mental and physcal fitness to control the population percentage of the ss fit more humanely and with less injury to man nd nature than is done by war.

Who are the wise and the honest in the population, and who am I to indicate who the wise and the honest might be? We usually regard as honest a person who does not knowingly tell or report as facts what he knows not to be so or who does not leave out in his speech or writing some essential which actually changes the meaning or significance of what he does tell or report. It is in this sphere that men in science have, or should have, greater experience, training, and conditioning than the rest of mankind, because the scientific method and scientific research demand absolute integrity, the absolute sticking to the facts as known or discovered. This does not mean that the scientific investigator is by heredity more honest than other fellow citizens. It merely means that science and dishonesty do not mix—they are incompatibles. The scientific investigator who lies is soon found out and discredited by his fellow workers. It is less easy to do such checking, such discrediting, in other fields of human endeavor.

This necessity for honesty, absolute personal integrity, and the reporting of all discovered facts as found without their being colored by wish or hope, should aid the scientist in following the same mental processes in the common life about him and in national and international affairs. I need not tell this audience that this does not always happen. After all, a scientist is a human being first and last and is subject to the same emotions, to the same national and international political pressures, fears, and hopes as are other human beings. All we can hope for ourselves is that we apply a somewhat larger element of the integrity, gained in science, in our common life as citizens of our nation and of the world.

The definition or designation of the *wise* is a more difficult task. That adjective implies wide factual knowledge and understanding, relative unselfishness, and a willingness to apply this understanding to problems where factual data are lacking. Human wisdom fails most conspicuously in passing judgment and acting on immediate needs, *and in neglecting the distant consequences.* This is intellectual shortsightedness—mental myopia. Man—that is, the human race—has dwelt on this earth at least a million years. It seems to me it is high time that those who would be wise should look ahead as to the consequences of their individual, national, and international actions, not only today and tomorrow, but a hundred, a thousand, a hundred thousand years ahead. As I see it, the person who has developed some control of his greed, his vanity, and his fears; who has developed to the limit of his brain the accumulated understanding of man and the universe, and who thinks in terms of his fellow men—the human race—not for the day, tomorrow, or even the next hundred years, but for a future at least as long as our human past; and who at the same time uses all his influence, without violence or coercion, to prevail on his fellow men to follow his example, is entitled to the connotation *wise.* We may then, even though dimly, select a standard and invite the wise and the honest to rally around it, even should this rally reveal but a corporal's guard in every land.

In my humble opinion the element in human nature and modern life forming the greatest obstacle to international peaceful cooperation, and hence the greatest force toward war, is dishonesty—lack of individual, national, and international integrity. This audience need not be told that guile, deceit, and double-dealing constitute the accepted international morality in all nations, though it is never put as honestly and baldly as I have just spoken. It usually takes the form of artistic lying. As long as this unfortunate behavior prevails among leaders in industry, trade, and politics, and in their international relations, it is difficult to see how genuine democracy can work, except by accident, or how genuine cooperation can be achieved in the international field. For example, we pretend to be shocked when it is reported as a "discovery" that other nations maintain spies in our midst. In spreading the publicity and pretended

horrors and wrath over such behavior, we forget to reveal that most, if not all, large nations, including our own, do just that thing in war and in peace. I, for one, fail to see how individual citizens in democratic nations or how individual nations in the United Nations can be held responsible for unwise, unfair, or violent actions when the political leaders in these nations and in the new United Nations do not put all the cards on the table, face up, as is done in science.

We Americans profess the ideals of democracy at home and endeavor to spread these ideals in other lands, and yet we agreed to set up in the United Nations a plan by which one of the five so-called great powers can block any action against the violation of the principles of democracy, justice, and fair play on the part of any one of these five larger nations. This is, of course, autocracy—not democracy, but perhaps this halting way is the only path for a hopeful start. I say "hopeful," because we must consider that some day in the future the leaders of these five great powers will be men of greater wisdom and integrity, men of wider and longer vision, than the political leaders in these nations today. When that day arrives, the responsible leaders will be superior to the present plan, and the plan itself will be a dead letter.

In my humble judgment the now defunct League of Nations failed to promote world peace and prevent the most devastating world war in human history, not so much because of faults in plans and powers of the League or because of the fact that our own country did not join the League, but because of lack of real faith in the League—that is, lack of integrity in the leaders of the dominant nations in the League. To them the League ideals and plans were just window dressings behind which the old game of national pride and national power politics went on as of yore. I fear seriously that this same lack of national and international integrity infests at least some of the leading powers of the United Nations. I see no other explanation of the supposed serious adherence of the five leading powers to this new international organization, parallel with the evident start of an individual armament race by the same major nations—an armament race starting, at least so far as plans go, before the guns of World War II even had time to cool. It seems clear to me that the United Nations' efforts toward world peace and the armament race and old-style military alliances of the five leading world powers are definitely incompatibles. International cooperation on the basis of the prevailing ethics of past and current international diplomacy is a delusion and a snare. Honest men with average understanding cannot even ho that it will be effective. Mr. Winston Churchill, author of the four freedoms of the Atlantic Charte now appears to identify peace with military for and he asks for military alliances against a resurge imperial aggression by Russia. We may well as Are military alliances in support of empires alread built by force any less injurious to the human ra than are such military alliances for building ne empires by military force? History seems to sho that, in the long run, neither are in the best interes either of the masters or of the slaves. The politica leader of a great and friendly nation said recentl that future peace demands that we treat our fello men in every land as brothers. At the very hour thi political leader made this humane and biologicall sound proposal his own soldiers were killing thei fellow men in the speaker's own imperial colonies Killing these people for what crimes?—for the crim of demanding the very freedoms which the people i the speaker's homeland achieved centuries ago. To me, this does not make sense. It adds up to lack o integrity, for this political leader is not a moron.

We Americans insist, and I think justly, that Japan give up all political and commercial control secured by force on the continent of Asia, but we are rather silent about Great Britain's control of part of China, a control also secured by force. We considered the Japanese control of islands in the mid-Pacific Ocean as a menace to our security. Now we propose to retain control of islands at the very door of China and of Japan. We insist that we are a peaceful people, yet we have waged three major wars in less than 50 years. Can we expect other nations to forget that fact? Is it not true that actions are more convincing than mere words?

Many fellow scientists and not a few citizens in the professions, in education, in industry, and in government appear to think that current false ideas and conceptions of *race* are serious causes of fear and hatred leading to violence and war. The science of biology and anthropology has clearly made out that, despite differences in skin color, anatomic details, language, culture, and religions, *the present human race on the face of this earth is biologically one species.* We have no sound scientific basis for the belief or the superstition of superior and inferior races of men. I am the last one to deny that the superstition of national inferiority or superiority has in the past been one of the causes of violence and war. But we have had civil wars in nations of very great racial homogeneity, nations with identical language, customs, religion, and traditions. We have had many wars between nations where there can be no question

fundamental racial differences, such as between rmany and England, Germany and France, Italy d France, Poland and Russia, China and Japan, etc., . The realization on the part of all men that the esent human race is one species will by itself not olish war. However, it should aid in this direction, d I should be the last one to minimize the impornce of this aid toward a more durable world peace. Many colleagues put great faith in better education, ore universal education of all people in every land, a prophylactic against future wars. As in the se of the problem of race and human unity, I ould be the last one to minimize the importance of ducation, particularly if this could embrace an underanding of the folly and the waste of war, the value d necessity of human cooperation and fair play, e immediate and the long-range injuries to man om modern wars. But education itself is not the re-all, is not the universal panacea. Men in every ation with the best education that modern underanding has been able to contrive have become war ongers and warriors by the old urges of greed, anity, fear, and actual or alleged industrial needs. However, education rather than propaganda is one f our means towards a better day, and we should ive our fullest support to the United Nations' Educational, Scientific, and Cultural Organization. It is obvious, however, that this must be factual education rather than propaganda—that our cultural emissaries to other lands, or in the service of the United Nations, should look at themselves and their own nations in the mirror of current and past history as frequently as they look at the errors and mistakes of our fellow men in other lands. In the last 50 years men in the natural sciences have had no difficulty in understanding, in fully appreciating the efforts of, and meeting on common grounds with, fellow scientists from every nation of the earth. In the natural sciences, at least, we do not need so much additional practice in fair and humane international relations with our fellow scientists. In saying that, I do not point a finger at other fellow citizens with fewer international contacts than the natural scientists; for, after all, we meet on the common ground of controlled facts and checked experience, arrived at through human ingenuity, under conditions of relative freedom of the individual scientist. That does not apply to those who travel the international road to distant lands with commercial interests, conflicting national aims, or fossilized political theory.

Despite some acquaintance with history and considerable experience in peace and war in many lands, I may be off the beam when I say that modern industry itself is at times a potent cause of war. Such industries, developed in locations or in nations where raw materials must be secured from other lands, the products of the industry disposed of largely in other lands, and with a population in excess of the food resources of the country, obviously render the people in those countries dependent on peaceful cooperation or war with other nations. When competing industries develop in other lands, conflicts are inevitable, both as to the raw materials and as to fields of trade. Political and industrial diplomats usually camouflage these conflicts with more altruistic and palatable connotations. We now discern such conflicts in new regions as a consequence of the recent elimination of Germany and Japan from the industrial scene.

In addition to building springboards for war, modern industry, by literally turning the earth inside out at a rate to which living forms have never before been exposed, has created other hazards to man's health and welfare. The atomic bomb is the culmination, not the initiation, of these new and man-made enemies. Given facilities and freedom, medical and engineering science of tomorrow may master this most recent enemy of man.

If there be a third world war, bigger and better atomic bombs will wreck and retard our industrial civilization. But such a war will not obliterate our species; and, lest current fears make us forget, many civilizations of the past have decayed and disappeared without the aid of the weapons of modern warfare. Slavery, parasitism, chicks that chirp but do not scratch, are potent enemies of our race. War, violence, and atomic bombs are on the screen for the moment, but these are but some of our many enemies.

In the past, we in the natural sciences have regarded it as self-evident and obvious that discoveries in science are not for personal or national gain. Such discoveries are for the increased understanding and aid of mankind. Is this principle, is this philosophy, wrong? Is the black-out of this principle by war necessary? And if necessary in actual war, is the black-out necessary for individual national security for an indefinite period during peace? I raise the question because it is one now pending, particularly in our own country, and because it has significant meaning for the entire human race. If the principle of the black-out in science shall prevail in war and in peace, science becomes not an instrument of understanding but an instrument of additional suspicion and fear.

Our Association embraces all science, all American scientists, and not a few scientists in other lands and climes. No one scientist can speak for all men of science, but you are in a position properly to value,

if not condone, my insistence that next to man himself—that is, man's unchecked greed, vanity, and fear—disease is man's major enemy, at least until depletion of national resources for industry and insufficient foods loom larger on the distant horizon. As a biologist I deplore the diversion of tens of thousands of competent scientists and such large fortunes in human toil, past, present, and future, to devising better ways to kill and injure our fellow men, better ways to waste and destroy our natural resources by war, because the frontiers of biology and medicine are still so vast. We have scarcely made a dent in the matter of prevention of the hereditary defects of man, of cancer or virus diseases, of the preventable impairments of the aging citizen. It seems stupid to pause to kill and maim our fellow men when there remains so much worthwhile work to do toward developing a healthier, wiser, and happier man of tomorrow.

Unless guile is coequal with integrity in man's survival and progress, it seems obvious that integrity, cooperation, and approximate justice constitute the very warp and woof of the "standard" to which wise and honest men must repair. We certainly get nowhere with guile in the understanding and control of inanimate nature or in the understanding and control of heredity, health, and disease in living nature. We can, for a time, guide human action by guile and force. Some day our colleagues in the social sciences, by the methods and ethics known to work in the natural sciences, will provide man with data on human behavior which are as reliable and as unavoidable as are the confirmed data of chemistry and physics of today. When that day is here, guile and guess in human relations will surely recede, assuming that man of that era retains present mental capacities.

Science Legislation

On the Floor of the Senate

Howard A. Meyerhoff
Executive Secretary, AAAS, Washington, D. C.

On 19 March the Senate Committee on Military Affairs considered the Kilgore-Magnuson Bill, S. 1850, creating a National Science Foundation, and reported it out of committee. S. 1850 is now on the floor of the Senate.

It has taken seven months to compose a bill that meets the requirements of scientists, government agencies, and the small group of Senators actively interested in science legislation, and to get this bill through committee. Comparable delays in the Senate and in the House can be fatal, for a third of our Senators, and all of our Representatives, are understandably concerned with election problems back home. Congress is not going to remain in session any longer than it must. It certainly will not linger for the purpose of creating a National Science Foundation unless Congressmen know that some of the influential people in their respective districts believe that this is important and enlightened legislation, which should have their support in the present Congress and not a promise of support in the next session.

On 16 March Senator Thomas of Utah, chairman of the Committee on Military Affairs, addressed a meeting at which 19 of Philadelphia's scientific organizations were represented. Senator Thomas, who is a member of the AAAS, devoted most of his time to a discussion of the significance of S. 1850 when he talked to the representatives of these organizations. Rather pessimistically, he pointed out the preoccupation of Congressmen with problems of re-election and ventured the prediction that S. 1850 can die in the Senate, and will almost surely die in the House—unless scientists show much greater interest than they have up to the present time.

Senator Thomas is so impressed with the wisdom of this bill that he pledged himself to reintroduce it in the next session, if it failed of passage this year. But failure this year means serious delay. It means that the teams of scientists who were at work during the war will become even more dispersed, more difficult to reassemble to pursue the research tasks of peace. Although scientists will appreciate the wholehearted support of Senator Thomas, it was clear from his remarks that they must assume a great deal of the responsibility for the ultimate passage of the bill, and practically all of the responsibility for its passage in this session.

Report on Science Legislation

Physical Society of Pittsburgh

(1) *National Science Foundation.* We believe that ere should be created an authority (National Sci- ce Foundation), hereinafter called the Organization, ose duty it would be to promote the fundamental d basic sciences in the interest of adequate national fense, of improved public health, of more effective e of our natural resources, and the increase of our ientific and industrial productivity in both quality d quantity.

(2) *Utilization of Existing Scientific Associations.* e believe that the Organization should make full use the many recognized scientific, technical, and engi- eering associations that have come into existence in is country during the past decades because we feel at the membership of those groups includes the more tive and capable of our scientific and technical eople.

(3) *Duty of the Organization.* We believe that the rimary duty of the Organization should be to foster e development of the so-called natural sciences, that physics, chemistry, mathematics, medicine, and biol- gy, to name a few.

We recognize the fact that a number of eminent people believe that the scope of a National Science Foundation should include not only the "natural sciences" but also the "social sciences," such as psychology, economics, sociology, political science, anthropology, and history, for example. However, we believe that the objectives and technics of research and development in the social sciences are so different from those customary in the natural sciences that investigations in the former field should be supported by a separate authority set up for the purpose and which would be coordinate in every way with the Organization herein proposed. However, in the event that a separate authority is not feasible, we strongly recommend that the support of social science research should be included among the duties of the Organization coordinate with that of the major divisions of the natural sciences.

(4) *Liaison Between Physical and Social Sciences.* We believe that an important function of the Organization should be the development of an effective liaison between those interested primarily in the natural sciences and those working in the social sciences.

(5) *Patent Policy.* We believe that the legislation covering the establishment of the proposed Organization should not attempt to change the present basic patent policy of the Government.

(6) *Selection of Governing Board.* We believe that it is of the utmost importance to have the Organization administered by men of the highest competence, completely independent of the influence of any special group. Although several types of organization could be set up to achieve this objective, it is our opinion that the work of the Organization should be administered by a Governing Board appointed by the President from a panel of scientific people recommended through existing scientific associations and that the Director of the Organization should be chosen by the Board and be responsible to it.

(7) *Compensation and Term of Office of Board Members.* We believe that the work of the Board would be of such magnitude, importance, and complexity that the members should give it their full time and should be paid accordingly. It is our opinion that the Board should be a continuing Board and that the normal term of office of individual members should be not less than six years. The Governing Board should be authorized to enlist the aid of qualified scientific advisers and be responsible for their remuneration.

(8) *Administration of Funds.* We believe that the Board should be entrusted with the administration of all funds appropriated to the Organization and with the award of contracts for research work, development work, purchase of equipment, modification of existing facilities or creation of new, and for such other purposes as might be necessary to the prosecution of investigations sponsored by the Organization in either nonprofit or industrial organizations.

(9) *Selection of Scientific Personnel and Projects.* We believe that the Organization should assist in the discovery and training of men and women possessing unusual abilities together with the special aptitudes necessary to creative scientific work in the fields of natural science research, and that to these

Many learned societies which customarily have not concerned themselves **with public affairs as distinguished from subject-matter studies have, in recent months, put time and energy into planning solutions of public problems of interest to scientists. This event alone is characteristic of our time and, as such, deserves notice in these columns. The views of every group taking concerted action cannot be mentioned here—but the official report of the Physical Society of Pittsburgh, one of the oldest physics groups of the country, accepted at its 200th meeting a short time ago might serve as a model to others whether they agree with the details or not.**

ends the Board should be empowered to award scholarships to selected students and grants-in-aid to individual science workers. We feel that the selection of scientific personnel and projects will tax the skill and vision of even the ablest Board and that on the wisdom of their choices will depend the long-range success of the proposed effort to improve the scientific stature of our nation.

(10) *Collaboration With Government Representatives.* We believe that government representatives, Naval, Military, and others, should cooperate with the Board in advisory capacities only; that it should be the policy of the Board to seek the advice of, and to collaborate with, such representatives; that there should be no ex-officio members on the Board and that no Board member should hold any other government or private position either elective or appointive.

(11) *Publication Policy.* We believe that the Board should be responsible for publication of technical reports covering the results of researches under its sponsorship either in existing scientific and te nical journals, in a publication of its own, or bo The Board should also be responsible for special pu lications designed to assist both the public and t Government to understand and apply effectively sp developments in the fundamental or basic sciences may arise from researches supported by the Orga zation.

(12) Finally, we believe that the powers vested the Organization as well as its basic policies shou be such as to assist the normal scientific activities either individuals or organizations. We wish strong to emphasize our conviction that the proposed Orga zation could best serve the nation by assisting in t creation of an environment favorable to independe thought and creative activity in the fields of bo fundamental science and basic technological develo ment, and by aiding the body politic to assimilate an benefit from the results of scientific achievement whatever their origin.

Obituary

Theodore Crété Burnett
1861-1945

Theodore Crété Burnett, associate professor of physiology, emeritus, of the University of California, died in Oakland on 18 December 1945, twelve days after his eighty-fourth birthday.

He was born in Brooklyn, New York, on 6 December 1861, of a family which had settled in Long Island in 1643. After private preparation he entered the College of Physicians and Surgeons of Columbia University and obtained his M.D. in 1887. He practiced medicine for a few years, but contracted tuberculosis and came to California to spend what his doctors had told him would be the last six months of his life. He began to recuperate and while in Mt. Shasta City met, during the summer holidays, J. B. MacCallum, the enthusiastic assistant of Jacques Loeb. Loeb had just been called to the University of California to head the Department of Physiology with the express purpose of organizing and directing research. Dr. Burnett offered his services as assistant without salary in the fall of 1903, and so began his association with the University of California. After Loeb's withdrawal in 1910, Dr. Burnett was placed on the staff as instructor and remained a teaching member of the faculty even after his retirement as associate professor in 1929, since he continued generously and voluntarily to assist in laboratory sections where help was needed until about 1935. He eventually made his home i Carmel, California. As he approached his eightiet year, his health began to fail, and he was virtually confined to his bed for the past three years.

Dr. Burnett's early scientific work shows the in fluence of Loeb. His first paper (1906) was entitle "The influence of temperature on striped muscle, and its relation to chemical reaction velocity," and his second (1907) attempted to answer the question: "Can sea water maintain the beat of the heart of fresh water animals?" For the next fifteen years one or more publications bearing his name appeared each year. About 1913 he became interested in the effect on cancer of such substances as lecithin, cholesterol, and extracts of the pituitary, much of the work being done in collaboration with T. B. Robertson. Experiments on liver catalase, begun in 1918, led finally to publication of work on the use of liver extracts in the treatment of hypertension in 1929. His last paper, which appeared the following year, was on the absorption of pituitrin by the stomach.

The passing of Dr. T. C. Burnett breaks the last direct link connecting the present generation of physiologists in the University of California with the period when Jacques Loeb gave such impetus here to original investigation.

J. M. D. Olmsted

University of California, Berkeley

Technical Papers

New Steric Effect in Organic Chemistry[1]

HERBERT C. BROWN

Department of Chemistry, Wayne University

Current theories of organic chemistry, particularly those developed by the English school (*5*), have emphasized the polar factor of substituents to the almost complete neglect of their steric factor. That is to say, these theories have sought to explain the effect of a given substituent by considering only the effect of that substituent upon the charge distribution within the molecule, without also considering the role played by the steric requirements of the substituent in altering the properties of the molecule.

In part, this overemphasis of the polar factor is to be ascribed to the disrepute into which the classical concept of steric hindrance had fallen as a result of its indiscriminate use by early organic theorists. These theorists found in steric hindrance a convenient explanation of phenomena which they could not readily interpret in terms of existing theory. Since these phenomena were drawn largely from the complex, little understood field of reaction rates, it is not surprising that a number of the phenomena so explained have since found other interpretations. It is unfortunate, however, that such errors led to the wide-scale abandonment of the concept and to its consequent neglect in modern theory.

Several years ago the author and his students embarked upon a program of study of relatively simple equilibria, the dissociation of molecular addition compounds, in the hope that these studies would yield unambiguous evidence upon which the concepts of steric hindrance and steric strain[2] might be firmly founded. The results already obtained offer strong support for the idea that atoms or groups of atoms through their steric requirements can exert marked effects upon molecular properties.

For example, if only the polar factor of alkyl groups were considered, it would be predicted that the strength of aliphatic amines should increase regularly with the number of alkyl groups: $NH_3 < RNH_2 < R_2NH < R_3N$ (Curve A, Fig. 1). However, the order actually observed is $NH_3 < R_3N < RNH_2 < R_2NH$ (Curve B, Fig. 1). (This discrepancy is discussed below.) In the absence of pronounced steric effects, the relative stabilities of the addition compounds formed by these amines with any given trialkylboron should exhibit the same order. This is true because the relative "strength" of the base (1) and the relative "stability" of the addition compound (2) can both be correlated with the relative tendency of the nitrogen atom in the amines to share its free electron pair.

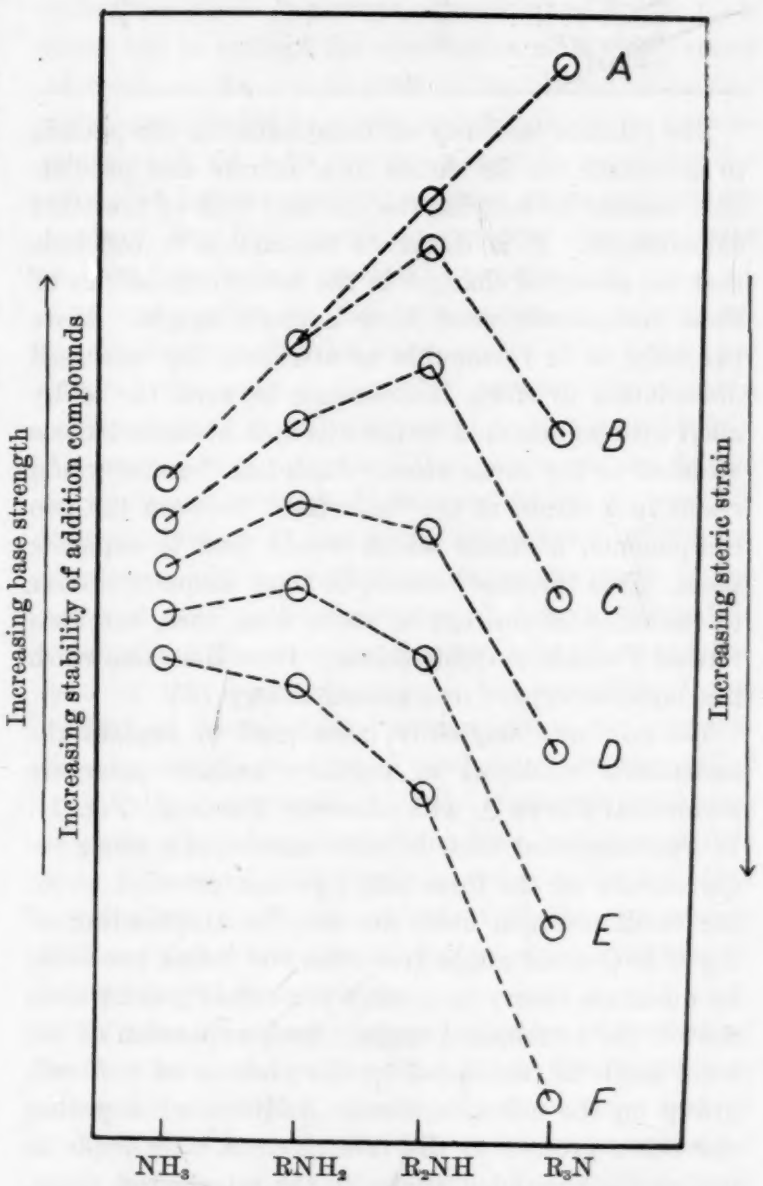

FIG. 1. Sequences shown by the aliphatic amines in comparisons of their base strengths and of the stabilities of their addition compounds with trialkylborons.

(1) $R_3N : H^+ = R_3N : + H^+$
(2) $R_3N : BR'_3 = R_3N : + BR'_3$

However, it has been possible to cause the observed order to vary from B to D, to E, and to F merely

[1] This research program at Wayne University on the effects of steric strains has been made possible by Grants No. 710 and 776 from the Penrose Fund of the American Philosophical Society. This assistance is gratefully acknowledged.

[2] The term "steric hindrance" is to be associated with a temporary condition in a reacting system; "steric strain," with an equilibrium condition in a relatively permanent system.

by increasing the size of the alkyl groups attached either to the nitrogen atom of the amine or to the boron atom of the other component of the addition compound (Fig. 1; Table 1) (*2*).

TABLE 1

SEQUENCES SHOWN BY AMINE SERIES WITH VARIOUS REFERENCE ACIDS

Amine series	Reference acid		
	H^+	$(CH_3)_3B$	$(t\text{-}C_4H_9)_3B$
Methyl	B	B	E
Ethyl	B	D	F
Isopropyl ...	B	E	
t-Butyl		F	

The relative tendency of these addition compounds to dissociate can be varied in a definite and predictable manner by varying the size and bulk of the alkyl substituents. It is therefore reasonable to conclude that the observed changes in the relative stabilities of these compounds must have a steric origin. More precisely, it is reasonable to attribute the increased dissociation to steric interference between the bulky alkyl groups attached to the nitrogen atom and those attached to the boron atom. Such interference would result in a strain at the "interface" between the two components, a strain which would tend to separate them. This "frontal" strain, in many respects similar to the classical concept of steric hindrance, has been termed F-strain to differentiate it from B-strain, which has no counterpart in classical theory (*3*).

B-strain was originally introduced to explain the anomalous weakness of tertiary amines (compare theoretical Curve A with observed Curve B, Fig. 1). It was suggested that, in such amines, the steric requirements of the three alkyl groups crowded about the small nitrogen atom are met by a spreading of the C-N-C bond angle from the 90° value predicted by quantum theory to a value somewhat greater than that of the tetrahedral angle. Such expansion of the bond angle is facilitated by the absence of a fourth group on the nitrogen atom. Addition of a proton (or other group) to the free electron pair tends to reduce the expanded angles to the tetrahedral value. This results in increased crowding of the three alkyl groups and the introduction of considerable strain into the molecule. This strain (called B-strain since it is localized at the "back" of the amine molecule) causes the amine to resist the addition of the proton (or other group) and leads to an apparent weakening of the strength of the base.

The hypothesis is strongly supported by observations on the behavior of phosphine and the methylphosphines. The greatly increased size of the central atom should result in the absence of B-strain. Experiment reveals that the base strength of these compounds increases regularly with the number of me groups, $PH_3 < CH_3PH_2 < (CH_3)_2PH < (CH_3$ (Curve A, Fig. 1) (*1*). The B-strain hypothesis of a reasonable, simple explanation for this marked ference in the behavior of the phosphorus and ni gen bases.

If three alkyl groups about a nitrogen atom br about a condition of strain, it follows from the el similarity in the dimensions of the two atoms t three such groups about a carbon atom should also a center of strain. This postulate offers a reasona explanation of many hitherto unrelated peculiari of branched-chain carbon compounds. A few of th may be briefly described.

(1) *Molecular rearrangements.* Alcohols with t structure R_2CHCH_2OH and R_3CCH_2OH exhibit marked tendency to undergo rearrangement in re tions involving removal or replacement of the h droxyl group (*6*). In such rearrangements either hydrogen atom or an alkyl group attached to t tertiary or quaternary carbon atom migrates. T marked lability of such groups is easily explicable terms of the strain postulated by the B-strain hypoth sis at such carbon atoms.

(2) *Hydrolysis of alkyl halides.* Ingold, Hughe and their co-workers have demonstrated conclusivel that tertiary halides hydrolyze by a mechanism in volving ionization of the halides as the rate-determin ing step (*4*). They have ascribed the greatly increase tendency of the tertiary halides to undergo suc ionization to the cumulative inductive effect of th three alkyl groups attached to the carbon atom whic holds the halogen. We wish to suggest that B-strain in the halide also facilitates the ionization, since such strain should be relieved by the expansion of the bon angles to 120° in the presumably planar carbonium ion.

$$R_3CCl = R_3C^+ + Cl^-$$

Indeed, a study of the effect of the size of the alkyl groups in such tertiary halides upon the rates of hydrolysis (recently completed at this university) has yielded results which would be exceedingly difficult to interpret without the aid of the B-strain concept.

(3) *Behavior of tertiary alcohols.* The unique properties of tertiary alcohols have never received an adequate explanation. According to the B-strain hypothesis, the strain resulting from the presence of the three alkyl groups furnishes a potent driving force to convert such alcohols to the relatively strain-free carbonium ions. Thus, reactions which involve carbonium-ion intermediates are greatly facilitated. Since the strain would also be relieved by the formation of the olefins, the marked tendency for such

pounds to undergo dehydration is also in accord h the hypothesis.

4) *Selective dehydration of alcohols.* Dehydration alcohols, such as $R_2CHCHOHCH_2R$, involving the ssibility of loss of either an adjacent tertiary or an jacent secondary hydrogen atom invariably pro- ds by the first-mentioned path. Again, this is dily explicable in terms of the B-strain hypothesis. Recent work has shown that the presence of two y bulky groups attached to a single atom may be e center of marked B-strain. The instability of ch compounds as di-*t*-butylether and di-*t*-butylamine ascribed to this cause. A quantitative estimate of e B-strain in such compounds has recently been ade. Its magnitude, 5 to 7 kcal, is such as readily to count for the behavior of such substances.

It is believed that the B-strain hypothesis shows romise of being a fruitful unifying concept in or- anic chemistry. Experimental tests of the hypothesis e being prosecuted as vigorously as present condi- ons permit. It is hoped that these investigations will ssist in drawing the attention of organic chemists to he desirability of including in their considerations oth factors, polar and steric.

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The Detoxification by Acetylation of Soluble Antigens From *Shigella dysenteriae* (Shiga) and *E. typhosa*[1]

Henry P. Treffers

Yale University School of Medicine

The toxicity of available vaccines against typhoid and other gram-negative organisms has long been recognized as a serious defect, particularly under military conditions where the loss in personnel time due to vaccination reactions may be significant. Attempts to provide reasonable type-specific coverage against the more important dysentery organisms with polyvalent vaccines must also take into account the additive nature of the toxicities of the component organisms. The only solution at present is to reduce the amount of each component until the toxicity of the combination is within tolerable limits. Since the antigenic efficiency of a component is influenced by its concentration, it is obvious that additional injections must be made to reach a high level of protection, a procedure which apparently produces many administrative difficulties.

Numerous attempts have been made to detoxify either the whole organisms or selected antigenic fractions, but in spite of the application of a wide variety of reactions the loss in toxicity has almost invariably been accompanied by a corresponding decrease in antigenicity (*4, 6*). An exception may be noted for the action of ketene gas (*1*) on some gram-negative organisms, but this promising reaction does not seem to have been widely applied in practice.

In our studies on the development of a practical vaccine against *Shigella dysenteriae* (Shiga), we have favored the use of a soluble antigen—the somatic polysaccharide, or polysaccharide-protein complex (*6*). Although it was recognized that this might not be the only antigen responsible for protection, it was felt that elimination of less active components of the organisms might be advantageous, particularly if the material was to be incorporated into a polyvalent vaccine with the corresponding antigens of other members of the dysentery group. In searching for a method of detoxification we have noted the preparation by several workers of acetylated derivatives of bacterial polysaccharides (*3, 5*). Although quite complete chemical characterizations have been made, little or no data on the biological properties of the fractions are available, with the exception of the observation that acetylated antigens do not react well with antisera to the whole organisms.

We have therefore prepared a series of acetylated derivatives of the polysaccharide, or the polysaccharide-protein complex, of *Shigella dysenteriae* and of *E. typhosa* (Army strain 58) and have investigated their toxicity and antigenicity. The soluble toxic antigens were dissolved in a small amount of water, diluted with several volumes of pyridine, and allowed to react at room temperature with an excess of acetic anhydride. The general technique of Freeman (*3*) was followed, with the exception that samples were removed at shorter intervals, and the reactions stopped by pouring the aliquots into water. As acetylation proceeded, an increasing percentage of the antigens became insoluble in water.

In all cases even the water-soluble fraction isolated after the minimum time allowed for acetylation (1.5 hours) showed an appreciable decrease in toxicity over

[1] Preliminary report. The work described in this paper was done with the assistance of Miss Claire B. Abrams and Mr. Ben A. Rubin, under a contract recommended by the Committee on Medical Research of the Office of Scientific Research and Development, and Yale University. The experiments were begun under a similar contract with Harvard University.

that of the original material. The fractions water-insoluble after acetylation for 24 hours were the least toxic.

Toxicity was determined from the weight loss in mice. For a base line, six mice were given an intraperitoneal injection of 0.5 ml. of saline, which was the solvent or vehicle used for the other antigens, and the mouse weights determined daily. Other groups, of as near the same age and weight as possible, were given 0.5 ml. of antigen solution or suspension and the weights estimated in terms of percentage loss or gain from the control group. Four mice given 0.4 mg. of undetoxified Shiga soluble antigen all died; with 0.2 mg. ¾ died; with 0.1 mg. no deaths occurred, but there was a drop in weight which reached 13 per cent by the third day; with 0.05 mg. there was only a 6-per cent weight loss for three days.

At a greatly increased dosage (3.0 mg.) the 12 acetylated derivatives prepared from this antigen did not kill any of the 48 mice used. The weight losses of the injected mice varied from a maximum of 10 per cent for the less acetylated soluble fractions to zero for most of the water-insoluble fractions or more highly acetylated soluble fractions. By this method, then, the toxicity of many of the fractions was at least 60 times less than that of the original material.

Preliminary results with a small group of rabbits, which are especially sensitive to these toxins, indicate that a single injection of 0.005 mg. of the undetoxified Shiga antigen will produce a temperature rise of 2.7° C., with a characteristic initial leucopenia followed by a leucocytosis. On repeated injection, temperature rises as high as 3.6° C. have been obtained, with a leucocytosis of 36,000 after 18 hours. A sixty-fold larger dose (0.3 mg.) of the acetylated antigens produced responses which, for the less highly acetylated soluble antigens, were about equal to those given by 0.005 mg. of the toxic material, while the responses for the insoluble fractions were more moderate (temperature rises of 1.6° C., leucocyte counts of 12,000). The detoxification ratio of 60 or more for the most highly acetylated fractions was thus confirmed in these animals. It is possible that at least a part of the toxicity remaining in the soluble, less highly acetylated fractions is due to contamination with traces of the starting material, from which it is difficult to separate. The insoluble antigens, on the other hand, could be repeatedly washed free of soluble substances.

On intraperitoneal or subcutaneous injection into mice none of the acetylated fractions has yielded agglutinins for intact Shiga organisms, although these are readily produced by injection of the unacetylated, toxic complex. On first sight the fractions were thought not to be antigenic or, if so, of a specific markedly different from that of the unacetylated material. That the latter is the case is indicated by the fact that more extensive immunization of rabbits has given rise to antibody which precipitates with acetylated fractions, although it does not agglutinate the intact organisms.

Of greater interest is the observation that mice given three subcutaneous or intraperitoneal injections of 0.05 mg. of the acetylated fractions do show active protection against infection with live Shiga organisms administered intracerebrally by Dubos' method (2). The data for three independent series of experiments are summarized in Table 1.

TABLE 1

SURVIVAL RATES OF IMMUNIZED MICE AFTER INTRACEREBRAL CHALLENGE WITH LIVE SHIGA DYSENTERY ORGANISMS

Immunizing antigen, given in 3 doses of 0.05 mg. each	Survivals	
	Number	Per cent
None—controls	4/55	7
Unacetylated, toxic Shiga antigen	4/15	27
Shiga antigens acetylated 1.5–4 hr.	19/93	20
Shiga antigens acetylated 5–24 hr.	64/151	42

It may be noted that the figures tabulated are for pools of animals; in some groups immunized with a particular fraction the survival rate was somewhat better (5/8), but the data for the smaller numbers of animals are not as significant statistically as are those for the combined groups. In a single experiment in which the challenge dose was administered intraperitoneally with mucin, 29 of the 61 mice (48 per cent) survived, as compared with none of 16 controls.

It should also be noted from Table 1 that the protection afforded appears to increase with acetylation, from which it may be concluded that the observed protection is not due to contamination of the acetylated antigens with small amounts of unchanged starting material. The protection in terms of multiples of MLD's is not impressive when compared to those of typhoid or Flexner dysentery protection experiments, but it is not out of line with that obtained typically in experimental Shiga infections.

Preliminary experiments with the protein-polysaccharide complex of *E. typhosa* indicate that significant detoxification of that antigen also may be obtained on acetylation. In a toxicity titration of the original soluble antigen in mice, the LD_{50} lay between 0.3 mg. (1/5 deaths, with 12 per cent weight loss) and 0.6 mg. (8/11 deaths). However, none of the 18 mice injected with 5.0 mg. of the acetylated fractions died, although some fractions produced transient weight losses of 10–15 per cent. The order of detoxification is thus about the same as for the Shiga antigen. The

otective power against active infection with typhoid ganisms is now under investigation.

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n the Blocking Antibody and the one Phenomenon in Human nti-Rh Sera

PHILIP LEVINE and R. K. WALLER

Ortho Research Foundation, Linden, New Jersey

Recent findings by Race (*7*), Wiener (*8*), and Diamond (*2*) indicate the importance of the indirect test as evidence of active isoimmunization in Rh– mothers of erythroblastotic infants. According to Levine (*6*), only 50 per cent of Rh– mothers who recently delivered infants suffering from this hemolytic disease have active anti-Rh agglutinins in their sera. In the remaining sera which fail to agglutinate Rh– blood, antibodies are present which specifically coat the surface of Rh+ red cells, rendering them resistant to the action of potent anti-Rh agglutinins. Diamond and Abelson (*3*) found that these so-called "incomplete," "blocking," or "inhibiting" antibodies will agglutinate heavy suspensions of fresh blood in tests carried out on slides. Presumably, the determining factor is the use of serum instead of saline as the medium for the cell suspension (*9*).

These significant findings on the behavior of blocking antibodies were confirmed. However, Diamond's observation that blocking sera will agglutinate heavy suspensions of washed blood could not be repeated. In order to facilitate studies on the specificity of the agglutination reactions given by blocking antibodies, Diamond's method was modified by the use of a 2-per cent cell suspension in human serum and test tubes instead of slides.

In the course of these confirmatory tests additional observations were made on the properties of those anti-Rh sera which exhibit the so-called zone phenomenon. Obviously, these sera contain both anti-Rh agglutinins and blocking antibodies, but the concentration of the former is greater. By and large, such sera were not considered as useful diagnostic reagents unless the agglutinin in a particular serum was far more active than the blocking antibody. However, the experiments presented indicate that at least some of these sera can be absorbed with Rh+ blood, so that after the blocking antibody is specifically removed the treated serum becomes a useful diagnostic reagent.[1] A typical experiment, given in Table 1, was carried out with the same serum originally described as exhibiting the zone phenomenon.[2]

TABLE 1

	Serum Sil.* Diluted 1:									
	2	4	8	16	32	64	128	256	512	1,024
Untreated	tr	±	+	+	+±	++	+±	+	±	0
Absorbed at 37° C.	+++	+++	+++	++±	++±	+±	+	±	0	0
Absorbed at 0° C.	+++	+++	++±	++	+±	+±	+	+	±	0

* The serum of patient Sil. was drawn in July 1942, and tests indicated in the table were carried out in July 1945. The undiluted serum was absorbed with an equal volume of washed sediment of Rh+ blood at both 37° C. and 0° C., but the agglutinin activity of the absorbed and unabsorbed sera were tested at 37° C. with 2-per cent saline suspension of Rh+ blood.

The test shows a somewhat higher titer with the serum absorbed at the lower temperature. Presumably, a slight quantity of the agglutinating activity was absorbed at 37° C., along with all of the blocking antibody.

Similar results were obtained with two other anti-Rh sera, one of which gave only doubtful reactions in the course of the titration. On absorption at 0° the two sera had agglutination titers of 1:32 and 1:16, respectively. The corresponding titers, after absorption at 37° C., were 1:2 and 1:4.

As was to be expected, the absorption mixtures with undiluted serum exhibited no gross agglutination; this was a favorable circumstance, because unagglutinated cells present a much larger surface area for specific absorption than agglutinated cells. This view could be confirmed in parallel absorption tests of pure anti-Rh agglutinins which require several treatments for complete absorption, whereas blocking antibodies of identical degree of activity were almost completely removed by one absorption.

The result presented in Table 1 could be duplicated in tests with a mixture consisting of equal parts of an anti-Rh_0 serum with agglutinating activity and another serum containing only blocking antibodies. On absorption of this mixture, which simulates to a remarkable degree the so-called zone phenomenon, it was possible to recover a great deal of the agglutinating activity (Table 2).

[1] After these experiments were completed, reference was found to similar absorption tests carried out by Wiener (*8*), but there is no indication that he tested the activity of the resfdual agglutinins by titration.

[2] The serum used in this test did not exhibit the zone phenomenon when first studied in July 1942. On standing for several months in the ice chest the serum was no longer found to be useful for routine testing because it exhibited the zone phenomenon to a striking degree (*5*).

The results indicate a slight, but distinct, zone effect in the mixture absorbed at 0° C. To a more striking degree the same effect was observed in mixtures of the same blocking serum with each of two other potent anti-Rh_0 agglutinins. This effect is probably due to incomplete absorption of the blocking antibodies in the mixture at the lower temperature. On absorption at 37° C., the blocking antibody was removed completely, but at the same time, there was a slight, but definite, loss of agglutinin titer. Nevertheless, the treated serum is still useful as a diagnostic reagent.

TABLE 2*

Serum	Diluted 1: 2	4	8	16	32	64	128	256	512	1,024
1	+++	+++	+++	+++	++	++	++	+	tr	0
2	0	0	0	0	±	+	++	+++	+++	+++
1 + 2, aa	0	0	0	ftr	±	+	+	±	ftr	0
1 + 2, absorbed at 37° C.	+++	+++	+++	+	±	tr	0	0	0	0
1 + 2, absorbed at 0° C.	+	++	++	+++	++	+	±	0	0	0

* Absorption of mixture of Sera 1 and 2 with equal volume of washed sediment of Rh+ blood. The titrations were tested with a 2-per cent saline suspension of Rh+ blood. Serum 1 is a pure agglutinating serum• (anti-Rh_0). Serum 2 is a "pure" blocking serum. The readings given for Serum 2 were made after the addition of a 1 : 10 dilution of a potent anti-Rh_0 serum. The result indicates a blocking antibody titer of 1 : 64–1 : 128.

Anti-Rh sera exhibiting the zone phenomenon behave somewhat differently in specific absorption at 37° and at 0° C. If the absorption of the blocking antibody is complete at the lower temperature, the treated serum is apt to give higher agglutinin titer than that shown by the serum absorbed at 37° C. On absorption at the higher temperature, the blocking antibody is removed first, and if this absorption is complete, some of the agglutinin activity may also be lost. Accordingly, one can expect to find for each serum a dosage of the absorbing blood which, under certain conditions, will remove all of the blocking antibody without influencing the agglutinin titer to any great extent.

Without carrying out absorption tests, it is difficult to state how often anti-Rh sera contain both blocking antibodies and agglutinins. The authors studied several sera with such concentration of the two antibodies that, even on titration, only traces of direct agglutination could be observed. Unless these tests are read microscopically, the weak degrees of agglutination in the higher dilutions could readily be overlooked. Furthermore, it seems probable that routine titration tests will entirely fail to detect those sera containing weak agglutinins and strong blocking antibodies. These views could be substantiated in experiments on mixtures of an agglutinating serum and excess of a blocking serum. Although no zone effect could be obtained on titration, absorption of the diluted mixture with Rh+ blood yielded a fluid which had strong agglutinating activity.

It is significant that in the observations reported the tests were carried out with diluted cell suspensions in saline. Under these conditions, specific absorption of certain anti-Rh sera reveal the presence of agglutinins even in the presence of strong blocking antibodies.

These findings have some bearing on the nature of the agglutinating activity of blocking sera, and the available evidence indicates that this agglutination is a manifestation of the blocking antibody per se. This could be determined in a few instances by titration results of blocking sera diluted in normal human serum instead of saline. These tests were carried out not only on slides with heavy suspensions of unwashed blood, but also in test tubes with 2-per cent cell suspensions in serum. The results with the latter modification provide proof that the slide agglutination does not depend upon the use of a "large number of red cells to absorb the inhibiting substances (blocking antibody) and to combine with agglutinin in sufficient number to form easily visible clumps" (*3*). As first suggested by Wiener, the essential mechanism in the slide test as direct evidence of blocking activity is the use of serum as the medium for suspending the Rh+ red cells. In further support of this view is our failure to obtain a positive slide test with the use of washed blood.

In contrast to the observations on the slide test is the finding that the agglutinin in a particular anti-Rh serum masked by an excess of blocking antibody can be studied quantitatively by the usual procedures after specific absorption of the blocking antibody.

From a practical standpoint, the significance of these findings lies in the fact that the characteristics of the agglutinating antibody and the blocking antibody are sufficiently clear-cut so that, for example, there is no difficulty in the use of an anti-Rh serum which contains an anti-Rh′ agglutinin and also an anti-Rh_0 blocking antibody.

Addendum: After this paper was submitted (August 1945), several important studies on the characteristics of blocking antibodies have appeared (*1, 4, 10*). The use of the term "conglutination" suggested by Wiener for the test with serum-suspended cells was criticized by Coombs, Mourant, and Race. One of the objections is based upon the presence of a heat-labile "conglutinating" complement.

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elapses Following Delayed Treatment Naturally Induced *Vivax* Malaria Pacific Origin

ARRY H. GORDON, LT. COL., M.C.; ALEXANDER MARBLE, COL., M.C.; WILLIAM W. ENGSTROM, CAPT., M.C.; HENRY A. BRUNSTING, CAPT., M.C.; and STUART W. LIPPINCOTT, LT. COL., M.C.

Army Service Forces, Eighth Service Command Harmon General Hospital, Longview, Texas

A most difficult problem in the treatment of *vivax* alaria of South and Southwest Pacific origin is the nbborn tendency of the disease to relapse. The act mechanism of relapse is not known (*9*), but the ggestion has been made that drug therapy which romptly and completely aborts the primary clinical ttack may inhibit the development of acquired im- unity (*8*). This, in turn, may be partially respon- ible for the relapse (*9*). Accordingly, it seemed easonable to consider that prompt therapy of acute ttacks such as soldiers obtain might be responsible for the large number of relapses, and to suggest the desirability of investigating the effect of withholding reatment if an opportunity arose (*6*). The estab- lishment by the Surgeon General of a center for the treatment of neurosyphilis at an Army hospital, to which large numbers of soldiers with relapsing *vivax* malaria had been admitted, has given an opportunity to study various facets of the primary attack of malaria. This report presents data on the effect of delay of institution of quinacrine therapy on the ten- dency to relapse.

Ten white soldiers with malaria, acquired in the South or Southwest Pacific, volunteered as the origi- nal sources for the infection of the American anopheline mosquitoes (*10*) used for natural induc- tion of the disease in 69 white soldiers who required malaria therapy because of neurosyphilis. The ad- ministration of quinacrine dihydrochloride (2.8 grams in 6 days) was delayed until the patients had had from 8 to 15 paroxysms with an average of approxi- mately 40 hours of fever over 104° F. This level was reached on the average in approximately 20 days, during which blood smears were positive for malaria parasites. The patients were then followed either until a relapse occurred or for at least 60 days with- out a relapse. Thick smears of the blood were ex- amined twice weekly for parasites during the period of observation, except during an interval of three weeks of furlough immediately after completion of quinacrine therapy. None of the patients received antiluetic therapy with heavy metals during the period of observation for relapse.

It is seen in Table 1 that 45 patients (65 per cent) have had a relapse. There were no significant differ- ences between the mean hours of fever above 104° or between the mean days of parasitemia in those patients who relapsed and those who did not. Of 16 patients observed following quinacrine therapy of the first relapse, 11 (69 per cent) have had a second relapse. In a group of 124 patients who contracted *vivax* malaria in the same overseas areas and whose relapses at Harmon General Hospital were treated promptly with quinacrine, 92 (74 per cent) relapsed. Relapse rates of 70, 76, and 77 per cent following

TABLE 1

RELAPSES FOLLOWING QUINACRINE TREATMENT OF *Vivax* MALARIA OF SOUTH OR SOUTHWEST PACIFIC ORIGIN

	Delayed treatment of first attack of mosquito-induced therapeutic malaria		Prompt treatment of relapses of naturally acquired malaria	
No. of cases	69		124	
No. of relapses	45*		92†	
Per cent relapse	65		74	
Time to relapse in days‡	Relapses Number	Per cent (Cumulative)	Relapses Number	Per cent (Cumulative)
Less than 29	2	4	6	7
30– 59	32	76	45	55
60– 89	8	93	21	78
90–119	2	98	12	91
120–149	0	..	3	95
150–179	0	..	5	100
188	1	100	..	...
Total	45	100	92	100

* Average period of observation of nonrelapsers in days: 109 (range, 66–185).
† Average period of observation of nonrelapsers in days: 143 (range, 62–353).
‡ Calculated from time of completion of treatment.

prompt treatment of initial attacks have been reported by Dieuaide (*3*) for three organizations serving over- seas. The differences between the rates of relapse following prompt and delayed treatment can hardly be considered of practical significance. Such a result was to be expected from the findings of Boyd and Kitchen (*1*) that there was no relationship between the duration of illness prior to therapeutic termina- tion of the primary attack and the rate of relapse.

Seventy-six per cent of the relapses which devel- oped within the period of observation following de- layed treatment of the patients with mosquito-induced

therapeutic malaria occurred within 59 days, and 93 per cent within 89 days following completion of quinacrine treatment. In the patients with naturally acquired malaria, 55 per cent of the observed relapses occurred within 59 days and 78 per cent within 89 days. This apparently longer period to relapse in the group with the naturally acquired disease may be due to the fact that the latter patients had had an average of eight relapses before inclusion in the study. For 9 of the 11 patients with induced malaria who had a second relapse following prompt treatment of the first relapse, the interval to the second relapse was from 6 to 52 days longer than the interval from treatment of the primary attack to the first relapse. For 1 patient, the interval was only 2 days longer, and for 1 patient 11 days shorter. The interval between first and second relapses averaged 22 days more than the interval between the primary attack and the first relapse for these 11 patients.

Relapses occurred in men infected with 7 of the 10 "strains" used. With 3 of the strains no relapses occurred, but only 7 men had been infected by these strains. Thirty-three of the neurosyphilitic soldiers were infected with the "Chesson strain" (Ehrman, *et al., 10*), and 25 (76 per cent) had relapses. Although these strains yielded so many relapses after induction of the disease by the bites of mosquitoes, it is noteworthy that in 28 men inoculated intravenously with 5 to 7 cc. of blood containing trophozoites of the same strains of malaria, none have relapsed during a period of observation averaging 106 days and ranging from 66 to 165 days. The importance of the route of inoculation in deciding whether the disease produced is of a relapsing type has previously been noted by James (*5*), and its relation to the production of exoerythrocytic schizonts has been discussed by Porter and Huff (*7*). Evidence that the source of the malaria is also important in determining the rates of relapse (*4*) is suggested by the fact that in 16 soldiers in whom *vivax* malaria of Mediterranean origin was induced by mosquito bites, only 2 (13 per cent) have relapsed to date. These relapses occurred at 111 and 189 days after completion of quinacrine therapy. The period of observation for the 14 patients who did not relapse ranged from 66 to 162 and averaged 113 days.

Although prolonged activity of the infection undoubtedly influences mechanisms of both cellular and humoral immunity (*2*), there is no evidence in this study to support the suggestion that early treatment may delay the development of "immunity" to malaria as measured solely by the incidence of initial relapses. A further delay in administration of quinacrine, perhaps until spontaneous remission, may be associated with a lower rate of relapse. Such rigorous management does not, however, seem justified, since the natural course of the disease is toward eventual cure even with prompt therapy of acute attacks (*3*).

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U. S. News and Notes

Dr. Joseph Hughes will succeed the late Dr. Harold D. Palmer as professor of psychiatry at the Woman's Medical College of Pennsylvania. Since 1943 Dr. Hughes has served with the U. S. Navy. At present he holds the rank of Commander and is chief of the neuropsychiatric service at the Philadelphia Naval Hospital.

Frederick L. Knowles, senior biophysicist, National Institute of Health, has been named editor of the *Journal of the National Malaria Society,* succeeding Dr. R. B. Watson, formerly with the Tennessee Valley Authority, who has joined the staff of the International Health Division of the Rockefeller Foundation. The *Journal* is a quarterly devoted exclusively to malaria and its associated problems. Subscriptions are $3.00 per year and may be obtained through Dr. Martin D. Young, P. O. Box 1344, Columbia, South Carolina.

Dr. Frithjof Setter, until recently immunologist and biochemist in the Michigan State Department of Health Laboratories, has joined the Technical Staff of Parke, Davis and Company, Detroit, as assistant to the director of the Biological Manufacturing Department.

Dr. Samuel L. Meyer, assistant professor of botany the University of Tennessee, has been appointed ociate professor of biology at Emory University, orgia. Dr. Meyer has recently been discharged m the Army.

Dr. H. M. Weaver, senior administrative assistant d assistant professor of anatomy, Wayne Univer- College of Medicine, Detroit, has been named sistant to the medical director of the National undation for Infantile Paralysis.

Dr. G. D. Shallenberger, professor of physics, and airman of the department, has returned to Montana ate University after seven months service with the rmy Educational Program in Europe. He served Shrivenham, in Marseilles, and in Frankfort.

President Karl T. Compton, of Massachusetts Insti- te of Technology, was awarded an honorary degree engineering from Worcester Polytechnic Institute, here he delivered the Seventy-seventh Annual Com- encement Address on 23 February.

Dr. Albert C. Spaulding has been appointed assis- tant curator in charge of the anthropological collec- ions at the Museum of Natural History of the Uni- versity of Kansas, with the additional title of in- structor in anthropology. Dr. Spaulding has had three years in the Government services.

Dr. Roy L. Whistler has resigned as chief of the Starch Structure Section at the Northern Regional Laboratory and has joined the Purdue staff as assis- tant professor of agricultural chemistry. He will con- tinue research on the chemistry of carbohydrates.

Dr. F. H. Winslow, formerly associated with the Manhattan District Project, and R. D. Heidenreich, formerly of the Dow Chemical Company, have become members of the technical staff of the Chemical Lab- oratories of Bell Telephone Laboratories, Murray Hill, New Jersey.

Announcements

The Du Pont Company has announced plans to award more than twice as many university fellowships this year as in 1945. The chemical industry today is facing a serious shortage of chemists, physicists, and engineers with advanced training. To help meet this problem the Du Pont plan provides for 41 postgrad- uate fellowships in chemistry, 5 in physics, 15 in chem- ical engineering, and 7 in mechanical engineering. Six postdoctoral fellowships in chemistry also are included in the enlarged fellowship program. Each postgrad- uate fellowship provides $1,200 for a single person or $1,800 for a married person, together with an award of $1,000 to the university. Each postdoctoral fellow- ship carries a stipend of $3,000, with an award of $1,500 to the university. The award of the $1,000 to the university in connection with the postgraduate fellowship and the $1,500 which accompanies the post- doctoral fellowship are intended to finance tuition and fees. The remainder of each fund is to be turned over to the department administering the fellowship for whatever purpose may seem desirable.

A New Department of Social Relations under the Faculty of Arts and Sciences has been established at Harvard University. This department will incorpo- rate all of the present Department of Sociology, that part of the Department of Psychology which has dealt primarily with social and clinical psychology, and that part of the Department of Anthropology concerned primarily with social anthropology. The new depart- ment is empowered to offer an undergraduate pro- gram of concentration in social relations, and graduate programs leading to the M.A. and Ph.D. degrees in sociology, social anthropology, social psychology, and clinical psychology. Instruction will begin in the Summer Term of 1946.

The personnel of the new department will include, from among the present Harvard staff, Talcott Par- sons, professor of sociology and chairman of the department; G. W. Allport, professor of psychology; P. A. Sorokin, professor of sociology; C. C. Zimmer- man, associate professor of sociology; Clyde Kluck- hohn, associate professor of anthropology; George C. Homans, associate professor of sociology; Robert W. White, lecturer in psychology and director of the Psy- chological Clinic; Stanley G. Estes, Thelma G. Alper, and Jerome S. Bruner, lecturers in psychology; Oscar Handlin, faculty instructor in social science; and James G. Miller, faculty instructor in psychology.

In addition, Samuel A. Stouffer, formerly pro- fessor of sociology at the University of Chicago and director of research in the Education and Infor- mation Division of the War Department, has been appointed professor of sociology and will join the department in September 1946.

A Psychology Section has been instituted by Dr. R. M. Page in the Fire, Missile and Pilotless Aircraft Control Division of the Naval Research Laboratory, Office of Research and Inventions, Washington, D. C. The Section, which will conduct psychological research on problems related to the design and operation of missile control equipment and on the training of the operators of these devices, includes: Dr. Franklin V. Taylor, formerly assistant professor of psychology, Princeton University; Dr. Alston S. Householder,

formerly assistant professor of biophysics, University of Chicago; Dr. Robert Y. Walker, formerly director of the Institute of Aviation Psychology, University of Tennessee; and Dr. Lloyd V. Searle, formerly assistant director of a wartime project of the National Defense Research Committee, Fort Bragg.

Applications for grants from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences should be received by the chairman of the Committee, Prof. Frederick G. Keyes, Massachusetts Institute of Technology, Cambridge 39, Massachusetts, not later than 15 April 1946. Grants are made in aid of chemical research, generally for apparatus or supplies, or for the construction of special facilities needed for research in chemistry or in fields closely related to chemistry. Grants are not awarded for salaries, and on account of limited resources, the amount to an individual is seldom in excess of $300. Application blanks may be obtained from the chairman upon request.

The American Society of Plastic and Reconstructive Surgery announces the publication of an official periodical to be known as *Plastic and Reconstructive Surgery*. The first number will appear in July, and the journal will be issued bimonthly. One volume of 500 pages will be issued each year, and the subscription price will be $6.00. Dr. Warren B. Davis, of Philadelphia, the editor, will have the assistance of a board of 12 associate editors. Subscriptions should be sent to the publishers, The Williams and Wilkins Company, Baltimore 2, Maryland.

Meetings

The Pennsylvania Academy of Science will hold its annual meeting Easter weekend, 19 and 20 April 1946, at Lehigh University, Bethlehem, Pennsylvania. Dr. Bradford Willard, of the Geology Department, Lehigh University, is president of the organization. The Academy was organized in 1925 and has a membership of over 600, most of whom are Pennsylvania scientists. The Pennsylvania Junior Academy of Science will resume its statewide meetings at the same time and place.

The Aero Medical Association of the United States will meet for its seventeenth annual convention at the Edgewater Beach Hotel, Chicago, on 7–9 April 1946.

The American Geophysical Union will hold its Twenty-seventh Annual Meeting in the Hall of Government, George Washington University, Washington, D. C., on 27–29 May. Information concerning the program may be secured from the office of the American Geophysical Union, 5241 Broad Branch Road, N. W., Washington 15, D. C.

Twenty-seven civilian and military electroencephalographers from several different states met at the Graduate Club of the Institute of Living at Hartford, Connecticut, on 1 March to organize the Eastern Association of Electroencephalographers. Formed for the purpose of promoting research in the field, the Association plans to pool scientific information concerning the neurophysiology and clinical application of electroencephalography.

Lt. Cdr. Robert S. Schwab, MC, USN, of the U. S. Naval Hospital in Boston, was elected chairman of the Association, and Dr. Charles W. Stephenson, of Hartford, was elected recorder.

One of the immediate projects of the group is to approach the American Physiological Society, the American Neurological Society, the American Psychiatric Association, and the Council of Physical Medicine of the American Medical Association, on the matter of establishing a joint committee among the several organizations for the purpose of considering the desirability and means of establishing minimum standards for approved electroencephalographic laboratories. Chairman of the committee appointed to pursue this project is Dr. Hallowell Davis, associate professor of physiology at Harvard; members are Dr. Paul A. Hoefer, associate professor of neurology at Columbia University, and Dr. Margaret Kennard, assistant professor of neuropsychiatry and neuroanatomy at New York University.

Elections

The Torrey Botanical Club announces the following officers for 1946: Dr. P. W. Zimmerman, Boyce Thompson Institute for Plant Research, president; Dr. John A. Small, New Jersey College for Women, 1st vice-president; Dr. Henry K. Svenson, Brooklyn Botanic Garden, 2nd vice-president; Dr. Jennie L. S. Simpson, Hunter College, corresponding secretary; Mr. Libero Ajello, Columbia University, recording secretary; Dr. Edmund H. Fulling, New York Botanical Garden, treasurer; Dr. Harold W. Rickett, New York Botanical Garden, editor; Mrs. Lazella Schwarten, Arnold Arboretum, bibliographer; and Dr. Anne M. Hanson, Columbia University, business manager.

Dr. Howard A. Robinson, chief physicist of the Armstrong Cork Company, was recently elected chairman of the Executive Committee of the Division of High-Polymer Physics of The American Physical Society.

International News

Dr. F. J. Belinfante, of the University of Leiden, been appointed associate professor in theoretical sics at the University of British Columbia, Van-ver. He will assume his duties in September 1946.

Dr. A. Velel Taning writes from Copenhagen how atly he appreciates the re-establishment of com-nication with other countries ". . . because I much oy reading articles and books from abroad after se many dark years, during which all connection h the civilized world was totally cut off. . . . We ceeded here in keeping the Dana Collections intact ring the war and we have published some papers the Dana Reports, which will be forwarded to the veral institutions in the near future. Very much aterial from the Dana Expeditions has been ar-nged for distribution to our collaborators abroad d papers from them are now coming in for print-g. This is a pleasure after these years lost."

Gunnar von Bahr, assistant professor at Upsala niversity, Sweden, has received a Government grant o study eye surgery in the United States.

Prof. J. P. Wibaut, of the University of Amsterdam, Holland, has written to M. T. Bogert, president of the International Union of Chemistry, as follows: "We have had very hard and difficult years, but we are thankful now to the gallant Allied Forces for our liberation. As long as it was possible there has been done much work in my laboratory."

Prof. J. Orcel, curator of mineralogy of the Museum National d'Histoire Naturelle at Paris, has written to Prof. Charles H. Behre, Jr., that his laboratories did not suffer materially from the occupation or from the war, though research of all sorts was—and still is, to some degree—greatly curtailed.

Dr. Antoine Ball, curator of insects in the Musée Royal d'Histoire Naturelle de Belgique, Brussels, wrote to Dr. P. P. Calvert on 7 December 1945, acknowledging receipt of publications sent and adding: "We have had a miserable time over here, but personally I am thankful to be able to say that none of my near relatives lost their lives on account of the war. The Museum sustained no damage."

The Moscow News of 12 December 1945 reports the death of Prof. Vladimir Leontyevich Komarov, president of the Academy of Sciences of the USSR and dean of Russian botanists, in Moscow in December. He was best known for his work on the flora of Kamchatka and as editor-in-chief of the *Flora* of the USSR, started in 1934, of which 10 volumes have been published to date.

Dr. Otto Rosenheim, London, in writing to Mr. Marvin H. Hack, University of Illinois, College of Medicine, says:

> There seems to be an air of mystery about the fate and whereabouts of German scientists of the prewar period. I have not heard anything about Klenk, who came to see me about ten years ago, when I presented him with some of Thudichum's preparations. Dr. Girard, of Paris, whom I met recently, informed me that Butenandt (Berlin) is working at present in Tubingen, in the French Zone of Occupation, and that Warbourg is back in Berlin after having fled to his villa in the island of Rugen. Wieland is supposed to be in Starnberg, near Munich, where his laboratory has been completely destroyed.

Prof. P. E. Verkade, Technische Hoogeschool, Delft, has written to Dr. Austin M. Patterson, Antioch College, that he has survived the war and his present address is 's-Gravenhage, Waalsdorperweg 88. He is chairman of the International Committee on Organic Chemical Nomenclature of the International Union of Chemistry, of which Dr. Patterson is the American member.

Dr. E. Leloup, Musée Royal d'Histoire Naturelle de Belgique, Brussels, has written to Dr. E. S. Deevey, Jr., Woods Hole, Oceanographic Institute, that he has been able to continue his work on hydroids during the war and he also said that Prof. A. Billard, the French student of hydroids, died two or three years ago of pneumonia.

Dr. Ing. Boh. Ma Mařan, director of the Institute for Forest Research, Prague XIX, Na Cvičišti 2, Czechoslovakia, writes to Dr. H. A. Lunt, of the Connecticut Agricultural Experiment Station, that he has had no contact with scientists in this country for the past seven years and is very eager for bulletins, reprints, and reports of progress pertaining to forest research, including forest soils.

Dr. Quido Zaruba-Pfefferman has written to Prof. Charles H. Behre, Jr., from Prague that many colleagues in geology are no longer alive. Among the deceased are Prof. Francizec Ulrich, Dr. R. Novacek, and Prof. Rosicky, executed in the concentration camp at Mauthausen. However, Prof. Slavik, the oldest professor of the Karlova University, Prague, returned safely after three years in the Buchenwald concentra-

tion camp. Prof. Kettner, who was in the United States at the time of the 1934 International Geological Congress, survived the German occupation.

Dr. Erna Mohr, curator of fishes, Hamburg Museum, has written to C. L. Hubbs, of The Scripps Institution of Oceanography, as follows:

> The sand eels for your museum have been burned, our Syngnathides, Centriscides and Echeneides too, but all the other fishes (in the Hamburg Museum) are safe. We must work hard to regain a library. In better times I must ask you to help us in this task. . . . I'm so sorry to hear that J. Norman is dead. Duncker, aged 75, is quite agile. Please give my best wishes to Herre and Myers!

Steps to explore the raw materials in India capable of producing atomic energy and to study methods of harnessing them were taken by the Board of Scientific and Industrial Research of the Government of India at their last meeting in New Delhi in January. The governing body of the Board set up a committee under the chairmanship of Dr. H. J. Bhabha, F.R.S., to explore the availability of raw materials in India capable of generating atomic energy, suggest ways and means of harnessing them, and keep in touch with similar organizations in other countries. The other members of the committee are Dr. Sir S. S. Bhatnagar, F.R.S., Dr. K. S. Krishnan, F.R.S., Dr. M. N. Saha, F.R.S., Dr. D. N. Wadia, Dr. Nazir Ahmed, and Dr. Jivraj Mehta. The governing body also set up a committee with Sir S. S. Bhatnagar as convener, to work out in this connection a program of research on beryllium and its master alloy.

Dr. F. P. Koumans, Leiden, has written Dr. Carl L. Hubbs giving further news regarding ichthyologists and fish collections. Dr. Koumans himself has just returned to Leiden from Copenhagen, where he spent a month recovering his health.

Of the Dutch ichthyologists Prof. Beaufort, Amsterdam, Prof. Delsman, Hilversum, and Dr. Havinga are well. Dr. Redeke died in the Spring of 1945 at the age of 71. Dr. Jan Verwey, formerly of Batavia and more recently director of the Zoological Station at Den Helder, is well. The building at Den Helder was damaged, and the whole institution was evacuated in 1940 to the Leiden Museum, to return late in December 1945, after the Station was partly repaired. Dr. Koumans knows of no ichthyologist in Belgium since the death of Giltay, of Brussels, in 1937.

Very little is known of German ichthyologists or institutions, as communications are not yet re-established. The museum and library at Hamburg were ruined, but the collections partly saved. The Berlin Museum is partly ruined, and the Senckenberg Museum in Frankfurt totally destroyed. It is not known what became of the collections. Ahl, of Berlin, is said to have been wounded in the war. Kiel is damaged that the university was brought to Flensburg.

The National Institute of Sciences of India, Bangalor, which has recently been recognized by the Indian Government as the primary scientific organization in the country, at their twelfth annual meeting passed a resolution favoring strict international control of atomic energy by a World Peace Organization. Following is the text of the resolution:

> Fellows of the National Institute record it as their considered opinion that any attempt to keep future atomic knowledge a secret will not only fail in view of the fact that basic atomic secrets have already been disclosed, but will lead immediately to a dangerous armament race and ultimately to war. They are of the opinion that the only security for humanity against destructive use of atomic weapons is to be found in setting up an international organization which will promote free exchange of all basic knowledge between scientists of all nations to ensure its use only for peaceful ends. The National Institute will give support to any international organization of scientists which may be formed for the purpose of bringing to the attention of all peoples and governments the necessity of placing atomic energy developments exclusively in the hands of such a world organization.

The Boca del Río Health Center and Tropical Medicine Training Station was formerly inaugurated on 21 February by the President of the Republic of Mexico, General of the Division Manuel Avila Camacho. He was accompanied by the Minister of Health and Welfare, Dr. Gustavo Baz; the Minister of Public Education, Mr. Jaime Torres Bodet; the Minister of National Economy, Ing. Gustavo Serrano; the Minister of the Navy, General Heriberto Jara; the Governor of the State of Veracruz, Mr. Adolfo Ruiz Cortines; and many officials of the federal, state, and local services.

Addresses were made by Dr. Pilar Hernández Lira, Director of the Health Center and Tropical Medicine Training Station; Dr. E. Harold Hinman, Director de Cooperación Interamericana de Salubridad Pública and Representative of the Institute of Inter-American Affairs; and Dr. Gustavo Baz, Minister of Health and Welfare.

This training station will provide excellent opportunities for training and research in tropical medicine as well as in public health, and it is hoped that it will provide field facilities in these specialties not only for students but also investigators from Mexico and other countries in the Americas.

The Dirección de Cooperación Interamericana de Salubridad Pública, a cooperative health service established by the Secretaría de Salubridad y Asistencia

Mexico and the Institute of Inter-American Affairs, t and equipped the building.

committee appointed by the Board of Scientific Industrial Research, New Delhi, will undertake a ematic examination of the radioactive contents of erals occurring in the different rock systems of India. This study is expected to be of help in understanding the chronological order of the great undated rock systems of the Deccan and the general geological layout of the Indian subcontinent. The knowledge thus gained will help mineralogists and prospectors in locating minerals and oils of economic value.

In the Laboratory

ssay of *p*-aminobenzoic Acid

DERROL PENNINGTON
University of Washington, Seattle

At the time Dr. J. C. Lewis published his micrological assay method for *p*-aminobenzoic acid (*3*), had developed a similar assay using a different ganism.[1] Since Lewis' method seemed admirable in l respects, and ours offered no unique advantage, r results were not published. In a recent private mmunication, however, Lewis stated that the organm used in his test, *Lactobacillus arabinosus* 17–5, ould be trained to give relatively stable *p*-aminobenoic acid nonrequiring lines by subculturing in the resence of suboptimal levels of *p*-aminobenzoic acid. He also reported that recently his stock culture gained he ability to dispense with *p*-aminobenzoic acid after maintaining a stable requirement for at least three years. The factors responsible for such changes have not been elucidated. In view of this and since other available methods (*1, 2, 4*) suffer either in convenience or sensitivity, it appears worth while to record that another organism, *Leuconostoc mesenterioides* Pd–60, is suitable for *p*-aminobenzoic acid assay.

In general, the basal medium and technique of Lewis' assay can be used with *Leuc. mesenterioides,* with the following differences noted. The assay tubes should be incubated at 37° C. for 15 hours. One-tenth millimicrogram of *p*-aminobenzoic acid per milliliter of medium gives maximum growth. The extent of growth must be determined turbidimetrically (*5*), since the organism does not produce large amounts of lactic acid. Samples of various natural products assayed with both organisms give comparable results. Representative values are given in Table 1.

[1] This work was done by the author while holding a postdoctorate fellowship from Swift and Company in the laboratory of Prof. Roger J. Williams, at the Biochemical Institute, University of Texas, in 1942. The author wishes to acknowledge the assistance of Miss Adele Neely in carrying out the assays.

The samples assayed were prepared by autoclaving 1-gram samples of the substance with 5 ml. of six normal sulfuric acids at 15 pounds pressure for 15 minutes. The samples were then neutralized with barium hydroxide, diluted to an appropriate volume, and filtered. Very little destruction of pure *p*-amino-

TABLE 1

Sample	*Leuconostoc mesenterioides*	*Lactobacillus arabinosis*
	micrograms per gram	micrograms per gram
Yeast	4.9	5.5
Wheat germ	1.7	1.7
Whole wheat	0.49	0.63
Egg	0.31	0.25
Banana	0.46	0.43
Peanuts, raw	1.6	1.7
Spinach	1.0	1.3
Beef liver	1.5	1.1
Beef muscle	0.04	0.05
Pork chop	0.34	0.26
Blood, human	0.03	0.04
Milk	0.05	0.03
Carrots	0.2	0.1
Potato, Irish	0.4	0.5
Sweet potato	0.09	0.06

benzoic acid was caused by this procedure, and maximum values were obtained in tissue extracts. Hot-water extraction or enzyme hydrolysis made available only a fraction of the total vitamin in the samples. Contrary to the findings of Lampen and Peterson (*1*), alkaline hydrolysis caused almost total destruction of the activity of tissue extracts, although the pure vitamin itself was not appreciably affected by that treatment. Tissue extracts were found to deteriorate rapidly on standing, even when kept frozen, and were therefore assayed on the day prepared.

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Antagonism of Salicylate by Pantoyltaurine

PHILIP G. STANSLY and CLARA M. ALVERSON

Chemotherapy Division, Stamford Research Laboratories, American Cyanamid Company, Stamford, Connecticut

Iványovics observed (*2*) that the inhibition of growth of *E. coli* and *Staph. aureus* in simple media by low concentrations (M/400–M/500) of salicylic acid was "specifically antagonized" by pantothenic acid and to a lesser extent by pantolactone. He concluded that under these conditions salicylic acid prevented the *synthesis* of pantothenate by inhibiting the formation of α, γ-dihydroxy-β, β-dimethylbutyric acid (pantoic acid). In a "complete" medium (*i.e.* one containing pantothenic acid or its precursor) *E. coli* is not affected by salicylic acid.

Pantoyltaurine, on the other hand, inhibits the growth only of certain bacteria (e.g. hemolytic streptococci) which require preformed pantothenate for growth. It has been considered that pantoyltaurine and other analogues of pantothenic acid act by interfering with the *utilization* of pantothenate (*3, 4*). It was suggested to us[1] that it might be possible to inhibit bacteria such as *E. coli* in a complete medium by some combination of salicylate (to prevent synthesis of pantothenic acid) and pantoyltaurine (to prevent utilization of preformed pantothenate).

Preliminary to experiments in a complete medium we wished to observe the effect of combinations of pantoyltaurine and salicylic acid on the growth of *E. coli* in a chemically defined medium, such as MacLeod's. It was found that whereas inhibition of growth was obtained with salicylate alone (confirming Iványovics), normal growth occurred with the combination of salicylate and pantoyltaurine. It was thus evident that pantoyltaurine, like pantolactone, antagonized the inhibitory effect of salicylic acid. Table 1 illustrates the antisalicylate effect of this compound. Other analogues tested in the same way (unpublished data) also showed an antisalicylate effect.

These findings suggested that pantoyltaurine is hydrolyzed, yielding pantoic acid which at pH 6.8 would exist as the pantoate ion (*1*). Assuming that hydrolysis of pantoyltaurine is the process involved, it may be calculated from Table 1 that hydrolysis of about 3 per cent could account for the observed effect. This figure was arrived at by considering that the "d" isomer of pantoate is the only active antagonist of salicylate and that pantoate is about nine times more active than pantolactone in antagonizing salicylate inhibition of *E. coli* (*6*). This should be considered an approximation in view of the errors involved in the type of assay illustrated in Table 1.

TABLE 1

ANTAGONISM OF SALICYLIC ACID INHIBITION OF *E. coli* BY PANTOYLTAURINE

Conc. drugs × 10^{-3}M	10 mg. per cent salicylic acid plus		
	d(−) pantolactone	dl-sodium pantoyltaurine	taurine
2	+	+	−
1	+	+	−
1/2	+	+	−
1/4	+	−	−
1/8	+	−	−
1/16	+	−	−
1/32	−	−	−
1/64	−	−	−

Drugs: All drugs used were made up in distilled water, sterilized by filtration and serial, twofold dilutions aseptically made in the medium; medium: MacLeod's (5), 5 ml., final pH about 6.8; inoculum: 0.2 ml. of a 10^{-6} dilution of an 18-hour broth culture (MacLeod) per 5 ml. medium; incubation: 37° C.; + = growth visibly equal to controls without drugs; − denotes absence of visible growth after 3 days. In the absence of any salicylate antagonist, 10 mg. per cent salicylic acid prevented appearance of visible growth for at least three days. In the absence of salicylate, neither pantoyltaurine, pantolactone, nor taurine caused any inhibition of growth.

An alternative explanation for the antisalicylate effect of pantoyltaurine may be that the material was contaminated with the pantolactone used in its preparation. However, quantitative investigation of pantoyltaurine antagonism of salicylate, the details of which will appear in a later publication, does not support this view. For example, according to Table 1, about 25 per cent contamination of dl-pantoyltaurine with dl-pantolactone (which is extremely unlikely) would be required to give the observed effect. Furthermore, the fact that other crystalline and highly purified analogues of pantothenic acid also antagonize salicylate inhibition (unpublished data) suggests that contamination with pantolactone could not be the only explanation.

The data in Table 1, which indicate that a solution of pantoyltaurine contains pantolactone or pantoate, suggest that this analogue (and others which show an antisalicylate effect) would be at a disadvantage in inhibiting the growth of those organisms which can utilize pantolactone or pantoate for the synthesis of pantothenic acid. The amount thus synthesized might be of such an order that the resulting ratio of analogue to pantothenate would be less than that required to prevent growth. Whether this disadvantage is actually sufficient to account entirely for the inactivity of the analogues against such organisms is not known at this time. It should be pointed out that the reduction in analogue concentration which would

[1] By Dr. R. O. Roblin, Jr., of these laboratories. McIlwain (*Brit. J. exp. Path.*, 1943, **24**, 203) considered the possibility of a synergistic action of salicylate and pantoyltaurine on *P. morganii* and reported finding synergism under certain conditions. According to Iványovics (*2*), however, salicylate does not exert a specific antipantothenate action on *P. morganii*. He found that salicylate inhibited *P. morganii* only in high concentration and that the inhibition was not antagonized by pantothenic acid. He considered the inhibition in this case to be due to the protein-denaturing properties of salicylic acid.

lt from hydrolysis is negligible and would have le effect on the ratio (*4*), whereas the liberation pantoate would have a considerable effect.

These observations do not detract from the possible fulness of pantoyltaurine and other analogues of ntothenic acid against Group A streptococci and esumably other organisms which are incapable of ilizing, or cannot readily utilize, pantolactone or ntoic acid for pantothenic acid synthesis. As eady indicated, reduction of analogue concentration y hydrolysis) would be inconsequential. Furthere, the inhibition of growth of Group A streptoci, for instance, with pantothenic acid analogues is established fact.

Summary

Like pantothenic acid, pantolactone, and the pante ion, pantoyltaurine and other pantothenic acid nalogues of this type antagonize the inhibitory effect salicylate on *E. coli*.

It is suggested that the active antagonist in a solun of such an analogue is pantolactone or pantoate. hese (particularly the former) could conceivably be ntaminants of the analogues. However, the liberaon of pantoate by hydrolysis, appears to be a more kely explanation for the antisalicylate effect.

The presence of pantolactone or pantoate in a solun of pantoyltaurine and similar analogues of panthenic acid provides a possible explanation for the ineffectiveness of these drugs in inhibiting the growth of microorganisms which can utilize pantolactone or pantoate for the synthesis of pantothenic acid.

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Interference With the Antibacterial Action of Streptomycin by Reducing Agents[1]

Amedeo Bondi, Jr., Catherine C. Dietz, and Earle H. Spaulding

Temple University School of Medicine, Philadelphia

The authors have repeatedly observed that the antibacterial action of streptomycin is significantly reduced by incubation in an anaerobic jar. When filter-paper discs are saturated with streptomycin and placed on the surface of infusion blood agar plates inoculated with *E. coli*, the resulting zones of inhibition on plates incubated anaerobically are much smaller than those on the comparable aerobic plates. The reduced activity of streptomycin anaerobically is not due to better growth conditions, since *E. coli* produces its maximum growth when incubated aerobically. Similar results may be obtained with staphylococci and other species of bacteria whose growth is favored by aerobic incubation.

These observations seemed to us to be significant, and further studies were carried out, the results of which suggest that they may have some bearing on the antibacterial action of streptomycin.

Method and results. Duplicate sets of infusion agar plates containing 2-fold concentrations of streptomycin were inoculated with various species of bacteria. One set of plates was incubated aerobically, the other in the anaerobic jar by the palladium-hydrogen method as modified by Spaulding and Goode (*8*). Plates were read for evidence of growth inhibition at the end of 24 and 48 hours incubation at 37° C. Table 1 shows the results of these tests.

TABLE 1

Inhibition of Bacterial Growth by Streptomycin on Infusion Agar

Organism	Incubation	Growth* in presence of streptomycin; units/ml. of agar							
		None	1.0	2.0	4.0	8.0	16.0	32.0	64.0
E. coli-S	aerobic	4	4	1	–	–	–	–	–
	anaerobic	3	3	3	3	3	3	–	–
E. coli-M	aerobic	4	4	2	–	–	–	–	–
	anaerobic	3	3	3	2	–	–	–	–
S. aureus-SM	aerobic	4	4	1	1	1	–	–	–
	anaerobic	4	4	3	3	2	2	–	–
S. aureus #7739	aerobic	4	1	–	–	–	–	–	–
	anaerobic	3	3	3	3	2	1	–	–
S. paratyphi B	aerobic	4	4	4	3	–	–	–	–
	anaerobic	3	3	3	3	2	2	2	1
S. typhi-murium	aerobic	4	4	4	3	2	–	–	–
	anaerobic	2	2	2	2	2	2	1	–
Pneumo. Type I	aerobic	4	4	4	4	4	1	–	–
	anaerobic	4	4	4	4	2	1	–	–
Str. Hemolyticus C-203	aerobic	4	4	4	4	4	3	–	–
	anaerobic	4	4	4	4	3	1	–	–

* Readings made at end of 24 hours incubation; 48-hour readings were essentially the same.

Under anaerobic conditions the amount of streptomycin necessary to produce bacteriostasis was from 2 to 16 times greater than the comparable aerobic concentration. With one exception (*S. aureus*-SM), these results were observed only with organisms which produced their maximum growth on aerobic plates.

A similar experiment was carried out with extract agar. Although there was some evidence that the antibacterial action of streptomycin was greater on the aerobic plates, the difference was not large. It appeared that various reducing agents in the infusion medium played a role in inhibiting streptomycin anaerobically. The greater reducing power of infusion agar was evident from the observation that methylene blue in a concentration of 1:100,000 in this medium

[1] Streptomycin used in this study was generously supplied through the courtesy of Dr. D. F. Robertson, Merck and Company, Inc., Rahway, New Jersey.

was reduced during anaerobic incubation, while methylene blue extract agar plates similarly incubated were not reduced. The presence or absence of streptomycin had no apparent effect.

The anti-*E. coli* action of streptomycin was subsequently determined in tryptone and infusion broth containing cysteine or sodium thioglycollate (Table 2).

TABLE 2

THE EFFECT OF CYSTEINE AND THIOGLYCOLLATE ON THE ANTIBACTERIAL ACTION OF STREPTOMYCIN AGAINST *E. coli*

Inhibiting concentration of streptomycin	
Medium	Units/ml.
Tryptone*	1.0
Tryptone plus 0.1 per cent thioglycollate	2.0
Tryptone plus 0.1 per cent cysteine	64.0
Infusion†	16.0
Infusion plus 0.1 per cent thioglycollate	64.0
Infusion plus 0.1 per cent cysteine	> 128.0

* Difco tryptone 1.0 per cent.
† Veal infusion, 1.0 per cent tryptose, 0.03 per cent glucose.

Aside from the added SH compounds, infusion broth itself contains interfering substances, since 16 times as much streptomycin was necessary for bacteriostasis in the infusion control as in the tryptone control. The presence of cysteine increased the concentration required for bacteriostasis 64-fold in tryptone and at least 8-fold in infusion broth; the increase with thioglycollate was only 2- to 4-fold.

TABLE 3

EFFECT OF INORGANIC REDUCING AGENTS ON THE ANTIBACTERIAL ACTION OF STREPTOMYCIN AGAINST *E. coli*

Inhibiting concentration of streptomycin	
Reducing agent*	Units/ml.
Tryptone control	2.0
0.5 per cent sodium formate	32.0
0.05 per cent stannous chloride	32.0
0.05 per cent sodium bisulfite	32.0
0.05 per cent sodium hydrosulfite	16.0
0.5 per cent sodium thiosulfate	32.0

* Final concentration in tryptone broth.

The effect of cysteine on streptomycin could be due either to a reducing action or to some specific chemical reaction, especially with the sulfhydryl groups. The inactivation of penicillin (*2*) and other antibiotic agents (*1*) by cysteine is well known. The action of cysteine on streptomycin appears, however, to be different from that on penicillin, as was demonstrated in the recent report of Denkelwater, Cook, and Tishler (*4*), published while this manuscript was being prepared. These workers state that the inactivation of streptomycin by cysteine is reversible. Similar interference by sulfhydryl compounds with the antibacterial properties of mercurials (*6*) and quinones has been reported.

If interference with the activity of streptomycin by sulfhydryl compounds is due to reducing powers, other reducing agents should likewise interfere with its action. Consequently, various reducing agents have been tested. Each of the substances studied definitely antagonized the antibacterial action of streptomycin against *E. coli,* as shown in Table 3. It is evident that the antibacterial action of streptomycin is greatly diminished by a variety of reducing agents other than sulfhydryl compounds.

Discussion. Reducing agents definitely antagonize the antibacterial activity of streptomycin. Further work will be required, however, to determine the true nature of this interference. Whether it is due to a lowering of oxygen tension or to some specific chemical reaction or both acting simultaneously, is still unknown. The SH compounds and the inorganic reducing agents could function in either capacity. The reduction in activity of streptomycin in the presence of glucose, as reported by Waksman and co-workers (*9*), could be attributed to the reducing action of this carbohydrate.

It is entirely possible that this phenomenon is related to the mode of action of streptomycin. This antibiotic displays its greatest activity against bacteria which grow better aerobically than anaerobically, e. g. *E. coli, S. aureus,* and *Myco. tuberculosis.* None of the obligate anaerobes is susceptible (*7*). The antibacterial action of streptomycin may be due to its ability to block some enzyme system, oxidative in nature, which is essential only to the growth of susceptible aerobic bacteria, an enzyme system which anaerobes do not possess. If this is true, it is possible that the antagonism by the reducing agent is a specific effect upon this streptomycin-enzyme relationship rather than a direct effect on the streptomycin itself. In fact, addition of the SH compounds and the inorganic reducing agents to a concentrated solution of streptomycin (1,000 units/ml.) does not result in material loss of activity, although Denkelwater and co-workers (*4*) recently reported that this antibiotic in a lower concentration was inactivated by cysteine.

Certain other practical implications are worthy of note. It is conceivable that in certain parts of the body where organic reducing agents are present or where a low oxygen tension exists, larger concentrations of streptomycin may be necessary to inhibit the growth of bacteria. Elias and Durso (*5*) recently reported that typhoid bacilli were isolated from stools in spite of the presence of large concentrations of streptomycin. These investigators suggested the presence in the body of a substance inhibitory to strepto-

in. It remains to be seen whether these two nomena are related.

is evident that the choice of a medium is im- ant in assaying streptomycin and in determining susceptibility of bacteria to its antibacterial activ-

Because of its antagonism for streptomycin, infusion medium would be an unwise choice for purpose. Eventually one of these reducing agents prove helpful in testing the sterility of strepto- in solutions or in the culturing of fluids from ients under treatment. Cysteine may prove to be h an agent.

Summary. The antibacterial activity of strepto- in infusion agar plate cultures of *E. coli* and er bacteria is diminished by anaerobic incubation. e bacteriostatic activity of this antibiotic for *E. coli* reduced in the presence of cysteine, sodium thio- collate, stannous chloride, sodium bisulfite, sodium drosulfite, sodium formate, and sodium thiosulfate. ysteine was the most active of the agents tested. urther investigation is necessary to determine the ture of this interference. It is possible that this henomenon is related to the mode of action of strep- omycin.

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Water-level Regulator for a Series of High-temperature Water Baths[1]

I. I. Bezman and E. P. Barrett

Mellon Institute of Industrial Research
University of Pittsburgh

It was necessary in this laboratory to conduct a series of tests at 70° C., the nature of which required the use of water as a bath liquid. The tests were carried out in two water baths, and, as efficient covers for the baths were not feasible, the diagrammed system (Fig. 1), set up in less than an hour, served to maintain the levels in both baths to within ¼ in.

In operation, the reservoir bottle, located on a shelf above the water baths, is filled from a tap, J, by closing screw-clamps, I and I′, and opening clamp I″. After the reservoir bottle is filled, clamp I″ is closed and I and I′ are opened. Line D extends below the surface of bath B and serves as a delivery tube, while line E is the regulator and cuts off the supply of air to the reservoir, F, when it is reached by the water level in the bath. Siphon C keeps the level in bath A at the same level as that in B.

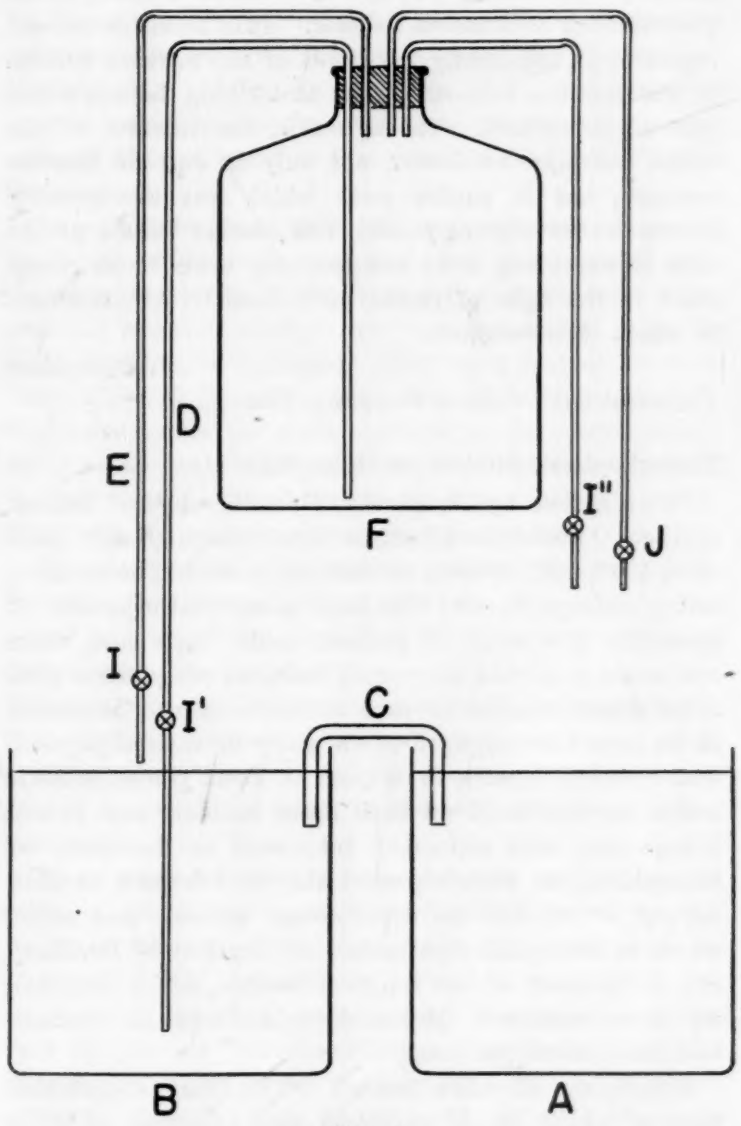

Fig. 1

The baths are of 6-gallon capacity, and the reservoir bottle holds 5 gallons. If the reservoir is filled in the late afternoon, this capacity is sufficient to make up for evaporation overnight. The tubes leading out of the reservoir are of glass, and the cork holding them is sealed in with DeKhotinsky cement. The siphon is of 15-mm. glass tubing to preclude stoppage by air bubbles.

With a sufficiently large reservoir, the system can be used to control a large number of baths. If the cost of the water is neglected, as it can be in most cases, this arrangement has a definite advantage over mineral oil baths in that cleaning of any glassware placed in the baths is much less troublesome.

[1] Contribution from the Industrial Fellowship on Optical Cements, Mellon Institute. Published by permission of the donor, Ordnance Department, U. S. Army.

Letters to the Editor

Soviet Scientists

The newly founded Institute of the History of Natural Sciences, USSR, has announced a publication program including such journals as *History of Russian Natural Science, Outstanding Leaders of Russian Science, Great Contributors to Russian Science.* This trend in science reporting is apparently the result of the wartime success of the Russian scientific work underlying industrialization of the USSR. Through this, the interest of the world has been awakened, not only in current Russian research, but in earlier work which was insufficiently known to contemporary scientists outside Russia at the time it was being done and has only come to be recognized in the light of recent more familiar achievements in which it culminated.

J. G. TOLPIN

Universal Oil Products Company, Chicago

Thromboplastic Studies on Hemophilia

In an article by Moldavsky, Hasselbrook, and Cateno, entitled "Penicillin effect on blood coagulation" (*Science,* 1945, 102, 38–40), the authors described some interesting findings, to wit: that after parenteral injections of penicillin in a series of patients under their care, there was noted a marked shortening in blood coagulation time after administration of that antibiotic drug. Inasmuch as we have been engaged in the study of various physical and chemical agents in respect to their thromboplastic action on the blood of both lower animals and human beings and were especially interested in the study of hemophilia, we have repeated the observations of Moldavsky, *et al.,* first on experimental animals and afterwards on hemophiliac patients. By courtesy of Dr. Howard Kern, chief of the Surgical Service, Sinai Hospital, we have confirmed Moldavsky's findings on normal-blooded clinical patients.

Employing Howell's method of studying coagulation time of whole blood, we found that injection of 2,000 to 5,000 oxford units of penicillin in medium-sized rabbits and cats produced definite shortening of coagulation time within two to three hours after administration of the drug, either by intravenous route or by intramuscular injection, thus corroborating the very valuable discovery of Moldavsky, *et al.* We have then made some studies, on two hemophiliac subjects, with intramuscular injections of penicillin. One of these subjects is a young man of 18 years, the other a man of 43 years, both of them having a normal coagulation time ranging from two to three hours.

To our great surprise we discovered that in neither subject was there noted any appreciable diminution in coagulation time after injections of quite massive doses of penicillin. One of the men received 50,000 oxford units, while the other subject was studied on two occasions, receiving 50,000 and 70,000 oxford units, respectively; in neither case was any effect produced on b coagulation two and one-half hours after injectio the penicillin. In view of the clinical findings of davsky, *et al.* on the one hand, and our own anima periments on the other, these findings in hemophilia be of interest in regard to its mechanism, which as remains an inadequately solved physiological proble

We have, however, been much more successful in po fully accelerating coagulation time of hemophiliac b by means of suitable deep X-rays. The most effe radiations in this respect were obtained by rays from K.V. apparatus operating on 20 M.A. and passed thr a composite filter of 2 mm. Cu at a target distance o cm. Specimens of hemophiliac blood *in vitro* expose from 60 r to 80 r, clotted in one-half to one-third of original time. Similar results *in vivo* were obtained the two hemophiliacs mentioned above by giving th deep X-ray radiations over the splenic region. T thromboplastic effect of the irradiation persisted fo long as 10 days. A detailed report of these studie to appear in the *Southern Medical Journal.*

Of interest also are experiments performed by us *vitro* with certain snake venoms on hemophiliac blo It is already known that the venom of Russell's vip (*Daboia*) hastens coagulation of such blood. We ha found in addition that the venom of the South Americ viper (*Bothrops jararaca*) is equally efficacious in th respect. Both of these venoms *in vitro* in concentratio of 1: 100,000 to 1: 200,000 may produce a solid cl with hemophiliac blood in five minutes. Of course the venoms cannot be employed therapeutically by parente injection, but they may prove useful for local applicatio

DAVID I. MACHT, M.D., F.A.C.P., an
MARCUS OSTRO, M.D.

Departments of Pharmacology and Radiology
The Sinai Hospital, Baltimore

The Presumptive Identification of Antibiotics

In the field of antibiotics a problem exists, the solutio of which would, we believe, benefit all those engaged i it. This problem concerns the presumptive identity o nonidentity of an antibiotic with one already reporte in the literature.

The most satisfactory way of determining the natur of an unknown agent is to determine its physical and chemical properties and compare it with known agents Unfortunately, for reasons well known to workers in antibiotics, it is frequently not feasible to do this. In the first place, the required data for comparison are rarely available. In the second place, the necessary purification may be extremely laborious. It is, moreover, of crucial interest to the investigator to determine the presumptive identity or nonidentity of his antibiotic *in a very early stage in the investigation.*

the present time, the only general means available establishing presumptive identity or nonidentity of antibiotic with reported agents, disregarding the al cases where some unique property of an anti- can be utilized, is the so-called bacterial spectrum. believe that the use of the bacterial spectrum for purpose has a number of disadvantages: (1) It re- s a considerable number of different types of organ- ; (2) unless the organisms are standard, easily ined strains, a comparison of literature values of known antibiotics with the values for the unknown t is subject to much uncertainty; and (3) as a lt, a satisfactory comparison of the unknown anti- ic with known agents requires the test to be carried simultaneously with the known antibiotics. The r, however, are frequently unavailable. With these iderations in mind, the following approach is sug- ed as a possible solution to the problem presented. n describing a new antibiotic, the investigator should rmine, under defined conditions, the relative inhibi- effect of his antibiotic on two strains of each of two ies of bacteria. One strain of each species should the parent, susceptible to the antibiotic. The other uld be a strain "made" highly resistant to the nt. The two species should preferably originate from ndard bacterial strains. If possible, one species should a representative gram-negative organism, such as *E.* (A.T.C.C. 9637), and the other a gram-positive anism, such as *Staph. aureus* (A.T.C.C. 6538). The r strains should then be filed with a central agency h as the American Type Culture Collection so that y would be readily available.

An investigator confronted with an antibiotic whose ntity with certain reported agents is in question uld then compare the relative effect of his antibiotic the parent and the various indicated resistant strains btained from the central agency. For example, an anti- iotic is discovered which resembles subtilin in certain spects. If the unknown antibiotic is as active against strain of *Staph. aureus* (A.T.C.C. 6538) highly resis- tant to subtilin as against a normal strain of *Staph. aureus* (A.T.C.C. 6538), the conclusion is justified that the two agents are not identical. In many instances, however, it would be necessary to compare the inhibition ratio of the unknown antibiotic with the published value for the known antibiotic in order to interpret the results. If necessary, the test could be extended to eliminate other reported antibiotics. Armed with this knowledge, the investigator would be in a more favorable position to report on the possible nature of his antibiotic while the investigation is still in a preliminary stage.

PHILIP G. STANSLY

American Cyanamid Company
Stamford, Connecticut

Regional Research Stations in Basic Science

The proposals for federal support of scientific research embodied in S. 1850 should have the hearty support of all scientists. Senators Kilgore and Magnuson, and their colleagues, the sponsors of these proposals for the expansion of scientific research in the United States, are to be congratulated on the able way they have developed the program. I venture to propose, however, a slight addition, which I believe will help to achieve the objectives desired.

A station for research in basic science should, in my opinion, be organized in each state and territory. These basic science research stations should be supported both by federal and by state funds. They should receive the monies apportioned to the states under the present provisions of S. 1850. In addition, each state research station should receive from the state concerned an annual amount at least equal to that received from the Federal Government.

In each state where there is a state university the state basic science research station should be associated with the state university in the same way that the state agricultural research stations are now associated with the state agricultural colleges. Each basic science research station should be under the control of the same body that administers the state university. In a state where there is no state university the basic science research station could be administered by a state agency established for the purpose or assigned that duty.

The scope of the basic science research stations should embrace the whole field of science. Research in the social sciences would therefore form a proper part of the program of each station.

Substations for basic research could be maintained, if desired, at research centers situated at places within a state other than at the state university. Research grants also could be made to research workers at other institutions.

These proposed basic science research stations would serve to coordinate those researches sponsored by the National Science Foundation with the researches in progress at the universities. Possible duplication of effort would thus be avoided. Such stations also would tend to prevent the possibility or suspicion that the Foundation might come to dominate too greatly the scientific research of the nation. At the same time the Foundation would serve as a coordinating agency and would act in an advisory capacity to all the state research stations.

LEE R. DICE, *Director*
Laboratory of Vertebrate Biology, University of Michigan

Science—A Means to What End?

Suddenly—the "instinct" of self-preservation has invaded the field of physics. A physicist nowadays is like a small boy who has been playing baseball in the back yard of a friend and who has knocked a home run through the big window of the living room in the house of his friend's father. His triumph at baseball is suddenly confronted with another and quite different system of values, in terms of which his triumph is no more than a misdemeanor.

In the social, unlike the physical, sciences we have

always recognized more or less explicitly that science deals with means, not ends; that the ends, not the means, are the finally decisive factors; and that the ends must be conceded to depend on a system of values which cannot be determined by scientific method but which rest on the nature, and immediately on the emotional nature, of man. Among these values, these emotions, these "instincts," that of self-preservation has usually been put at the head of the list. Suddenly, after several centuries of apparent freedom from this impeding or limiting consideration, even the physicist—the most disinterested of scientists—has found that self-preservation is as intimate and inescapable a factor in his cosmogony as it is in that of the humble rodent.

Science is only a means to an end. Ah, but to what end? Is that not the first question?

C. REINOLD NOYES
455 East 51st Street, New York City 22

Remarks on "Science and Man's Dilemma"

There is a point in Bruce L. Melvin's impressive article (*Science*, 1946, 103, 241–245) on which I venture to take issue with the author. He mentions *domination* as a type of social behavior, and in effect proceeds to say that war, the desire for huge fortunes, the urge to surpass others are all basic in our economic, political, and social *systems*.

It seems to me that much turns on this idea, and that the idea is erroneous. It seems to me that war, the desire for huge fortunes, the urge to surpass others are not basic in our economic system. I think that they are basic in the *practices* that prevail in the system, that these practices are essential to much of the personnel that now dominates the system and are deemed so to more of it.

I think that this personnel is fearful of its position, that it senses unworthiness in itself, and that it turns against the system antagonism that it knows should be directed against itself and its practices. Its fear is increased by knowledge that its practices are, in fact, not essential to the system, but rather are detrimental. It tries to change the public idea of our system and to change our system itself, to its own advantage.

Its fear is further increased by knowledge that its practices are not essential to the general welfare and happiness or to the development of the best that is in the world and in men. It tries to make its practices essential to the welfare of individual persons, in order to provide for the continuance of these practices. It fears practices other than its own, knowing well that these might be to the good of the system as well as to the general good. Its great ally is material want, and it seeks to maintain this or to substitute, as may be possible. It desires continuance or discontinuance of any system according to its own chances of continuing in these practices, in which it has found itself to excel.

It talks freedom, competition, patriotism, fearing them all, and it talks teamwork—hoping to continue to drive the team. It looks toward an end of these practices as toward its own doomsday, as something to be put off as far as possible, come what come may. It wants f dom from fear—for itself only—and a beggar in country would be more sure to have it.

CARL D. MU
327 Salem Street, North Andover, Massachusetts

Reply to Dr. Asmous on Russia

It is surprising that in 1946 a letter similar to t of Vladimir C. Asmous could appear in a scient periodical (*Science*, 1946, 103, 281). It seems it d not contain facts but only feelings. In keeping with tendency of the latter I should like to express opinion, shared by many Americans, that the peo whose language Dr. Asmous "does not understand" h saved his life, as well as those of 130,000,000 oth citizens of this country. At least they have saved great troubles. They did it with an unprecedent amount of sacrifice and an unparalleled development science. And everyone, wherever he is in the world, w enjoys freedom and an opportunity to work in scienc is indebted to the 20,000,000 Russians who lost the lives in defeating consciously the Nazi tyranny. Ind vidual mistakes, failures, and tragedies are occurri everywhere and in all times. The leading artic "Science and Man's Dilemma," in the same number *Science* contains many amiable answers to questio raised by Dr. Asmous. It is well known that the Sovie scientists and people have shown on many occasions sin cere and friendly relations toward the American scien tists and people. A letter like that of Dr. Asmous cer tainly does not contribute to the friendship of tw nations.

In conclusion I should like to change the sentence o Dr. Asmous, "We are probably talking again differen languages although we both were born in the same coun try," as follows: All three of us were born in the *same* country, talked the *same* language, and breathed the *same* air but we have *different* feelings (at least two of us). And is it not the commonest fact (often an evil) in this incoherent yet attractive promising world of the human race?

SERGEI GAPOSCHKIN
Harvard College Observatory

Rediscovery of Vitamin A

Dr. Smith's letter (*Science*, 1946, 103, 281) raises an important point, namely, the difficulty of scanning the immense literature of biochemistry well enough to know whether an observation is a new discovery. The difficulty is intensified when the early work is in Russian or Japanese, for instance, with a long interval before revival.

My own "discovery" in 1936 of the ester condition of natural vitamin A was due to unfamiliarity with the field, since I had recently emerged as a biochemist after a training in photography and high vacuum. In a later paper (*Chem. Rev.*, 1944, 34, 95, sec. II, line 1) I mention my mistake and give credit to the earlier discoverers of the ester story.

The moral surely is that we must all—authors, editors, and printers—be very careful, making first reports as

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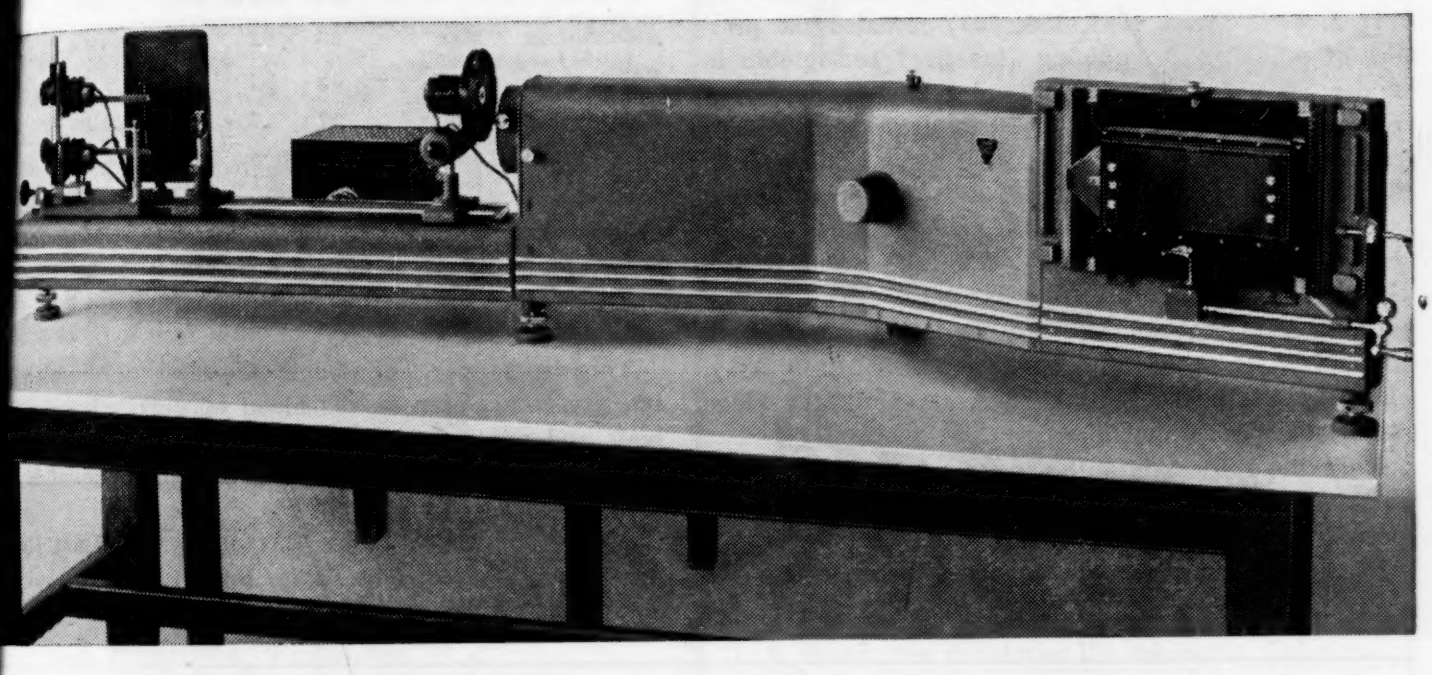

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accurately as possible and correcting errors as soon as discovered. With this in mind, *Science* may care to trade Messrs. Koscher and Barter for Kascher and Baxter, who were the actual authors of the article which raised Dr. Smith's ire. This will prevent a fourth (and imaginary) set of discoverers of the vitamin-A acid earth-blue color creeping into the literature.

K. HICKMAN

Distillation Products, Inc., Rochester 13, New York

[*Science* acknowledges the responsibility of introducing two fictitious investigators.]

Inactive (Non-oxygen-combining) Hemoglobin in the Blood of Ophidia and Dogs

The observations of E. Ammundsen (*Science*, 1939, **90**, 372; *J. biol. Chem.*, 1941, **138**, 563) revealed the presence of non-oxygen-combining (inactive) hemoglobin in 40 per cent of human bloods and in amounts varying from 2 to 12 per cent of total hemoglobin. Similar results were obtained by W. N. M. Ramsay (*Biochem. J.*, 1944, **38**, 470) in 17 horses, with a frequency of 82 per cent and a mean value of 8.4 per cent for inactive hemoglobin (ferrihemoglobin). In agreement with Ammundsen, Ramsay identifies the inactive hemoglobin as methemoglobin—an assertion not shared by W. S. Cox and W. B. Wendel (*J. biol. Chem.*, 1942, **143**, 331), who deny the presence of methemoglobin in the blood of various species, including man.

Since the subject is still a point of issue, it seemed worth while to extend these observations to other animal species, such as Ophidia and dogs.

In the experiments to be reported below, active Hb was determined by the oxygen capacity method of D. Van Slyke and W. C. Stadie (see Hawk and Bergeim, *Practical physiological chemistry*. (11th ed.) 193 total Hb, by the iron method of E. Ponder (*J. Chem.*, 1942, **144**, 333). The observed difference betw active and total Hb was attributed to inactive Hb.

The following table gives the values of inactive found in four species:

Author	Species	Number of animals	Number of blood samples	Inactive hemoglob Frequency %	Limits (g%)
Ammundsen (1941)	Man	53	82	40	2–12
Ramsay (1944)	Man	38	38	55	1.5–7
Ramsay (1944)	Horse	17	17	82	3.0–25.5
Prado (1944)	Jararaca	23	23	100	6.0–28
Prado (1945)	Dog	22	31	82	3.5–20.5

The table shows the impressing fact that in *Bothrop jararaca*, frequency (100 per cent) and mean quanti (17 per cent) of inactive hemoglobin are much great than in the other species.

This is, to our knowledge, the first observation o inactive hemoglobin in the blood of poikilothermic an mals and might be of some value in the study of th physiological significance of this unusual form of hem globin.

J. LEAL PRAD

Instituto Butantan, São Paulo, Brazil

Book Reviews

Animal breeding plans. (3rd ed.) Jay L. Lush. Ames, Ia.: Collegiate Press, 1945. Pp. viii + 443. (Illustrated.) $3.50.

This book continues to serve as a blueprint for improvement of animals through breeding. It is conveniently organized for a logical presentation of the subject, beginning with the background of animal breeding and the genetic principles which form a basis for scientific animal breeding. Breeding plans based on selection, relationship, and somatic likeness occupy a majority of the pages. Other pertinent topics concerning breeding plans and relating to reproduction are included.

Dr. Lush has been successful in presenting the genetic bases for animal improvement in a thorough and realistic manner. Necessarily complicated genetic explanations have not been avoided or oversimplified, but have been carefully clarified. Many of the principles developed by Wright, Fisher, and others are organized and discussed in order to make them more readily available to the student, research worker, and practical animal breeder. While this book serves as a text for undergraduate courses in animal breeding, it is well adapted to the use of graduate students and research workers. For the latter groups a more complete bibliography would increase its usefulness. The references are adequate for supplemental reading and, for some chapters, are arranged under subject headings so that the reader may readily choose those which fit his particular needs.

Commercial animal breeders who have an elementary understanding of genetics will find many aids to guide them in designing a breeding program which is most efficient for their conditions. They should welcome the realistic discussion of the rate of improvement which can be expected from various breeding plans and the clear statements of what each breeding method will and will not do in changing the genetic makeup of their herds.

Only minor changes have been made from the second edition. In general these involve the addition of recent references and are adequate in bringing the book up to date in most details. No mention is made of the

tice of selective registration by the Columbia Sheep ders Association since its organization in 1941, but program may be too recent to permit critical evalu- The chapter on sire indexes has been revised con- ably. The book is well printed and bound. The eet index appears to be adequate.

CLAIR E. TERRILL

D.A., *Western Sheep Breeding Laboratory*
ois, Idaho

elation of cycles in weather, solar activity, geomag- tic values, and planetary configurations. (1st ed.) axwell O. Johnson. San Francisco: Phillips and Van rden, 1946. Pp. viii + 149. (Illustrated.)

his book consists of numerous tables and graphs of fall, sunspots, planetary configurations, and other , with comments on the results. The author is con- ed that various cycles of considerable lengths in rs, which are related to configurations of the planets, demonstrated. He attributes the cycles in terrestrial nomena to cycles in solar variation, and these solar es to electric or magnetic influences of the planets. object in all this extensive computation and study o find sufficiently reliable cycles in terrestrial phe- nena to be of real value in forecasting yields of crops.

My own belief in the reality of certain periodicities in r variation inclines me to hope that predictions of ue may eventually be possible from studies of them. regret that all of Mr. Johnson's data are yearly mean lues. I think that it is desirable to have a more tailed basis, using monthly values, for the solar peri- icities I accept are not multiples of years.

C. G. ABBOT

mithsonian Institution, Washington, D. C.

tatistical methods: applied to experiments in agriculture and biology. George W. Snedecor. Ames, Ia. Iowa State College Press, 1946. Pp. xvi + 485. $4.50.

This is the fourth edition of this well-known work, hich has been widely used in the fields of agriculture d biological research since its first appearance in 937. The general order of presentation is the same as efore: simple variation and correlation, some large mple theory and more complex cases of chi-square, nalysis of variance and covariance, multiple and cur- ilinear regression, and more complex concepts. There has been considerable minor rearrangement, and new mphasis has been placed on sampling, fiducial limits, stimation, and components of variance. The format is omewhat more attractive than in previous editions.

The book begins with several new sections on sampling of attributes, considerably more imposing than the former very elementary opening. A table of fiducial limits for binomial material is introduced (its theory being left to Chap. 16). There is also a new and useful table of random numbers. Some of the ideas brought out in the former Chapter 1 are then developed. Other chapters show less difference from former editions, but in all there are changes. Graphic tests of significance

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are omitted from Chapters 2 and 4, and mathematical tests are treated more exhaustively. Fundamentals of regression and correlation are more fully discussed, and the Z-transformation is introduced. Chapter 9, on chi-square, contains some material originally in Chapter 1, as well as some new material. The chapters on analysis of variance contain material on basic assumptions, components, and disproportionate frequencies, not in older editions. Later chapters have fewer changes, but there is more attention to Gauss multipliers and more detail in discussion of single degrees of freedom, while the section on errors of ''betas'' is omitted. An obvious error in Example 14.7 is retained. Some familiar problems and sections are omitted and some new ones introduced.

These changes show the influence of development in the knowledge of statistics and of the work of associates on the strong staff at Ames. The book retains many of the characteristics of earlier editions. The informal language with its personal pronouns, adding to readability; the effort to develop logic ''painlessly''; the presentation of tables in a form to appeal to experimenters more than to mathematicians; the strong practical emphasis and wealth of practical problems are all there. Analysis of variance is strongly emphasized, and other techniques are related to it. The close relation of the author's laboratory to experimental work in various fields is well reflected. Difficult questions are handled in an apparently easy manner, reversing the practice in some texts.

The changes superimposed on the former development have made logical outlining a little difficult. The text is definitely more valuable as a reference than earlier editions and seems more difficult to adapt to teaching. In studying and using the text, the scientific worker will feel anew the influence of the modest and unselfish work of the author and his associates, which has already contributed so much to progress.

F. M. WADLEY

Research Administration
U. S. Department of Agriculture

Organic preparations. **Conrad Weygand. New York: Interscience Publishers, 1945. Pp. xiii + 534. (Illustrated.) $6.00.**

This book, authorized by the Alien Property Custodian, is an English translation and condensation of *Organisch-chemische Experimentierkunst,* which was published in 1938 by J. A. Barth in Leipzig. Conversion to the English idiom is satisfactory, and indeed the publisher's Preface cites nine persons as concerned in this task.

Only the second part of the three subdivisions of the original has been translated, the other sections, concerned with materials and operations (Pt. I) and ch cal analysis and physical characterization (Pt. I having been omitted. The part translated is that titled ''Reaktionen'' in the German edition. The p lem of classifying organic reactions and of correla them with laboratory practice is ever a difficult Prof. Weygand elected to make a classification ba upon the type of bond formed. This divorces the cla fication from the conception of functions and their activity, but probably gives a more systematic treatm of collective synthetic methods. One advantage of s an arrangement is that the classification of reacti by the name of their discoverer or, as is more often case, by that of their promoter, is distinctly subordinat Many examples of actual laboratory procedures tak from the available voluminous literature are cited. C densation has been effected in the translation by om ting the details but giving the references to procedur in ''Organic Syntheses.''

The Index, prepared by Mrs. Lucia Dawe, is great improved and extended from that of the German te and the detailed Table of Contents aids in locating particular reaction.

Apparently little effort has been made to revise t book to 1945 (excepting references to other books a to Organic Syntheses, the reviewer counted only fi literature references beyond 1937), and it therefore co stitutes an addition to the library of a book alread available in an idiom with which an organic chemi must perforce become familiar. The book will, howeve serve a useful purpose for students of organic chemistr who wish to familiarize themselves with organic sy thetic methods from either a theoretical or practic standpoint. Many students will use the present tran lation who would veer from the German edition. Th book is perhaps of more value for such a purpose tha as an authoritative reference book on synthetic proce dures. For example, the little section entitled ''Ether of Sugars'' (pp. 165–168) is pitifully incomplete, an actually most of this small space is devoted to glyco sides, which are not ethers at all, but acetals. The sec tion on glycol-splitting reagents (pp. 454–456) is like wise inadequate from the modern standpoint.

Nevertheless, this translation will be a valued addi tion to our American libraries. Its appearance move the reviewer to pose a problem. Is this book (and others like it) perhaps an intermediate phase in a future trend away from German to English supremacy in the organic monographs and texts? If so, a major task awaits the English-speaking authors, and at any event the vast accumulation of past work in German will still require familiarity with this difficult language.

M. L. WOLFROM

The Ohio State University

Scanning Science—

An Anthropological Club for informal discussion was formed in New York on March 4th. Some fifteen students of anthropology met at the house of Dr. Franz Boas and discussed the recent works on children and child psychology by Sully, Baldwin and Chamberlain, the books being reported on by Prof. Giddings, Dr. Frrand and Dr. Boas, respectively. No formal organization is proposed at this time.

—13 March 1896